UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

ARTEMUS BANKS, Plaintiff, v. BAXTER INTERNATIONAL, INC., a corporation; BAXTER HEALTHCARE CORPORATION, a corporation, and SCIENTIFIC PROTEIN LABORATORIES, LLC, a limited liability company, ROBERT L. PARKINSON, JR., JAMES M. GATLING, and DAVID ROHRBACH, Defendants.	)	Case No. 08-cv-02324 Hon. Judge Robert W. Gettleman Magistrate Judge Mason

PLAINTIFF'S RESPONSE TO DEFENDANT, BAXTER, ET AL.'S MOTION TO STAY

NOW COMES Plaintiff, ARTEMUS BANKS, by and through his attorneys, Nolan Law Group, and in response to the Defendant, BAXTER HEALTHCARE CORPORATION, ROBERT L. PARKINSON, JR. and JAMES M. GATLING's Motion to Stay Proceedings Pending Transfer to the Judicial Panel on Multidistrict Litigation states as follows:

1. Pursuant to Panel Rule 7.2 (i), Plaintiff will be providing a response of interested party to Plaintiff D'Amico's motion to consolidate the heparin related cases before one Multidistrict Litigation Court.

2. It is the Plaintiff's position that all heparin related litigation should be centrally located here in the Northern District of Illinois. The motion to consolidate the heparin related cases is currently scheduled to be heard before the Multidistrict Litigation Panel (MDL Panel) on May 29, 2008 in Ashville, North Carolina. Based on past

experience with MDL Panel decisions, it is likely that it will take two to six weeks for the MDL Panel to issue an order concerning the appropriate location for the consolidation of the heparin related cases. This presents the possibility that the MDL Panel will not issue an order until mid-July and regardless of whether the heparin related cases are consolidated pre-trial discovery may not commence until some time thereafter.

3. While the cases respecting the issuance of a stay order cited by the Defendants are well founded they fail to take into account the rather unique circumstances of the heparin related cases and the great potential for the Plaintiff to suffer undue prejudice should such a stay order be entered. Unlike many other product liability cases, this case is unique in that it involves a biological product (heparin is manufactured from the mucosal lining of pig intestines) that has a distinct expiration date.

4. On January 9, 2008, Defendant, Baxter, suspicious of a problem, placed its inventory of heparin on hold.

5. On January 14, 2008, Defendant, Baxter suspended its manufacture of heparin products.

6. On January 17, 2008, recalled a large number of lots of their heparin products based on widespread reported adverse reactions and death associated with the use of their heparin based products. Again on February 28, 2008, Defendant, Baxter, proceeded with broader recall of all of its heparin based products. Similar recall of heparin based products was performed by the Defendant, SPL.

7. As part of these recall campaigns, letters were sent to consumers of heparin as well as to wholesalers and distributors and other health care professionals. The consumers of Defendant, Baxter's, heparin product were instructed to discontinue use

and segregate the recalled product and then contact Baxter to arrange for the return of the product to Baxter. (See Exhibit A).

8. Baxter then received various quantities of recalled heparin from end users of the product or from its wholesalers and distributors.

9. Since the date of the initial recall, Defendant Baxter, has engaged in extensive testing of the recalled product as well as its heparin based products manufactured as far back as 2006. Baxter is conducting most of this testing here in Illinois and is also engaged in testing its recalled heparin in Europe. (See Exhibit B).

10. On April 21, 2008, Defendant, Baxter, issued a press release respecting some of Baxter's initial test results. Baxter determined that over-sulfated chondroitin sulfate ("OSCS") was the contaminant found in its product that is attributed to hypotensive reactions for the patient.

11. On April 23, 2008, the New England Journal of Medicine published its article, *Contaminated Heparin Associated with Adverse Clinical Events and Activation of the Contact System*. The New England Journal article authors arrived at similar results finding that OCCS cause adverse reactions in patients.

12. The primary problem with placing a stay on this case concerns the biologic nature of the product at issue. While it is known that OSCS is the likely contaminant that may be causing the adverse affects and death, what is not known is what will happen to the OSCS or the samples containing OSCS as time passes. On March 19, 2008, in an FDA media briefing, the FDA's Director of Center for Drug Evaluation and Research, Janet Woodcock, M.D., stated that: "It is most likely that ordinary chondroitin sulfate is chemically modified to create this compound that is found in the contaminant

[OSCS]. (See Exhibit C). Since OSCS was just recently discovered by be the ingredient that is used to taint the subject heparin, it is not yet known what effect the OSCS will have on the "shelf life" of the natural heparin product that it is mixed with.

13. On April 21, 2008, Dr. Woodcock stated that OSCS is "a modified naturally occurring product that has been chemically modified. And in its original form mimics the biological activity of heparin." (See Exhibit D). It is clear that a foreign product, OSCS, was introduced into Baxter's heparin in variable amounts and quantities that may have a significant impact on the stability of the end product heparin. The chemical and biologic stability and the speed at which the heparin and the OSCS will breakdown or decompose is currently unknown.

14. Even "pure" unadulterated heparin sold by Baxter has a one year expiration date. (See Exhibit E).Expiration dates are placed on each dosage of this biological product based on the probability that the product will not retain its sterility or the effective biologic properties of the product will decompose or breakdown over time. Under either scenario, the product's chemical and biologic properties are prone to change over time.

15. The initial recall concerned Baxter heparin manufactured in the fall of 2007. Even without the new concerns that OSCS brings to the stability of the subject heparin, the expiration dates for even "pure" heparin are fast approaching.

16. Also unknown is the ability to preserve the subject heparin to ensure an accurate test sample in the future. Baxter and SPL have had the luxury of being able to destructively test their product without any concerns for product sample stability or expiration. Until such time as the stability of recalled product is known no one, including

this Court, can state with confidence that a stay order in this case will not bring harm and prejudice to the Plaintiff.

17. The Plaintiff should not be placed in a position where, by virtue of a stay of proceedings, the Defendant, Baxter or SPL gains a tactical advantage and may attack the validity of testing performed by Plaintiff's experts not on their merits but on the technicality of "stale" samples that are only stale because the Defendant's made them so.

WHEREFORE, Plaintiff, ARTEMUS BANKS, prays that this Court deny Defendant, BAXTER HEALTHCARE CORPORATION, ROBERT L. PARKINSON, JR. and JAMES M. GATLING's Motion to Stay Proceedings Pending Transfer to the Judicial Panel on Multidistrict Litigation and allow Plaintiff to conduct limited discovery respecting the recall of heparin and testing of the subject heparin.

Dated: May 12, 2008

Respectfully Submitted,

/s/ Paul R. Borth, Esq.
Paul R. Borth
NOLAN LAW GROUP
20 North Clark Street, 30th Floor
Chicago, Illinois 60602-4109
Tel: (312) 630-4000
Fax: (312)630-4011

Attorneys for Plaintiff

CERTIFICATE OF SERVICE

I, Paul R. Borth, do hereby certify that on May 12, 2008, I caused a copy of **Plaintiff's Response to Defendant Baxter, et al.'s Motion to Stay** to be served on Defendants' counsel by electronically filing the foregoing document with the Clerk of the Court using the CM/ECF system which will send notification of such filing to:

Leslie M. Smith, P.C.
Kirkland & Ellis, LLP
200 East Randolph Drive
Chicago, IL 60601
Telephone: (312) 861-2141
Attorneys for Baxter Healthcare Corp., Baxter International, Inc., Robert L Parkinson & James M. Gatling, Defendants

/s/ Paul R. Borth, Esq.
Paul R. Borth, Atty. No.: 6226633
NOLAN LAW GROUP
20 North Clark Street, 30th Floor
Chicago, Illinois 60602-4109
Tel: (312) 630-4000
Fax: (312) 630-4011

EXHIBIT A

Baxter Healthcare Corporation 847.948.5811
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

Baxter

Urgent Product Recall

February 29, 2008

Re: All Baxter Heparin Products of the following sizes
Heparin Sodium Injection 1000 units/mL - 1 mL, 10 mL and 30 mL Vials
Heparin Sodium Injection 5000 units/mL - 1 mL and 10 mL Vials
Heparin Sodium Injection 10,000 units/mL - 1 mL and 4 mL in 5 mL Vials

Dear Renal Home Patient:

As a precaution, Baxter Healthcare ("Baxter") is expanding its **voluntary recall of Heparin Sodium Injection to include all lots of single and multi-dose vial products**, due to an increase in reports of adverse patient reactions including stomach discomfort, belly pain, upset stomach, nausea, vomiting/dry heaves, diarrhea, **decreased or low blood pressure,** chest pain, fast heart rate, dizziness, fainting, unresponsiveness, shortness of breath, feeling your heart beat strong or fast, drug ineffectiveness, burning sensation, redness of the skin, paleness of the skin, abnormal sensation of the skin, flushing, increased sweating, decreased skin sensitivity, headache, feeling unwell, restlessness, watery eyes, abnormal sensation of the mouth or lips, throat swelling, thirst, and difficulty opening the mouth.

Our records indicate that you may have received the Heparin Sodium Injection (1000 units/mL, 5000 units/mL, or 10,000 units/mL) product manufactured by Baxter that is affected by this recall.

Please check your supplies immediately to determine if you have any of the above Baxter Heparin products.

Please note, if you have received a recent shipment of Heparin from Baxter, it may be APP/Abraxis Heparin. **The APP/Abraxis Heparin is acceptable for continued use and is not being recalled; only the Baxter Heparin identified above is being recalled.** APP/Abraxis is an alternate supplier of Heparin with whom Baxter has partnered to provide our home patients replacement product.

If you have any Baxter Heparin product, **discontinue use of the product,** segregate that product and contact Baxter Dialysis Patient Services at **1-800-284-4060** to arrange for the return.

Baxter

Baxter intends to send every patient a replacement order of his or her existing Heparin prescription within the next 14 calendar days. The replacement order will not be Baxter Heparin; it will be APP/Abraxis Heparin. We are working as quickly as possible to send these replacement products to each patient. However, if you have a concern regarding continuing your therapy until you receive the replacement product, please contact your dialysis center for further instruction.

Please complete the attached reply form confirming your receipt of this letter and return it to Baxter using the enclosed addressed and postage-paid envelope. Baxter is required by the FDA to obtain responses from our customers on notifications of this nature. Returning the form promptly will prevent you from receiving an additional notice.

We appreciate your immediate attention and apologize for any inconvenience this may cause you.

The FDA has been notified of this communication.

Sincerely,

Raymond Godlewski Sr. R.Ph.
Vice President, Quality
Baxter Pharmaceuticals and Technologies
Baxter Healthcare Corporation

Baxter

HOME PATIENT REPLY FORM
URGENT PRODUCT RECALL
February 29, 2008

Urgent Product Recall Applies to All Products Listed Below:

Heparin Sodium Injection 1000 units/mL - 1 mL, 10 mL and 30 mL Vials
Heparin Sodium Injection 5000 units/mL - 1 mL and 10 mL Vials
Heparin Sodium Injection 10,000 units/mL - 1 mL and 4 mL in 5 mL Vials

Please complete and return this record to us either using the self-addressed stamped envelope attached or by FAX to 1-847-270-5457.

Patient Name and Address: *(Please Print)*	
Reply Confirmation Completed By: *(Please Print Name)*	
Telephone Number: *(Including Area Code)*	

☐ I have the product affected by this recall in my possession and have contacted Baxter to arrange its return.

☐ I have no product affected by this recall in my possession.

Signature/Date:
REQUIRED FIELD _____

EXHIBIT B

Baxter

UPDATE ON INVESTIGATION
March 5, 2008

Baxter's first priority is ensuring that its products are safe. In keeping with this priority, Baxter is in pursuit of the root cause of the increase in the allergic-type reactions associated with its heparin sodium vial product to understand the underlying reason(s) for the increase in adverse events that it has seen with its heparin product, and is committed to making sure this critical product is available for all of the patients that need it across the United States. Its scientists and expert consultants have employed a battery of sophisticated analyses to methodically isolate and rule in or out the multiple variables in the manufacturing process and supply chain.

The following is a preliminary update on the status of the company's investigation into the root cause of the increased allergic reactions associated with its heparin product, as well as background information on the product, its manufacture and supply chain.

Update on Investigation and Findings

At this point, Baxter has ruled out the manufacturing process at its Cherry Hill, New Jersey manufacturing facility as a potential contributor to the root cause. The investigation into the elements of Baxter's manufacturing process included an analysis of the components that make up the heparin solution and its packaging (the vial, rubber closure, water, sodium chloride and benzyl alcohol), an extensive evaluation of the data collected during manufacture of the products, and a review of the aseptic processing conditions at the time the products were manufactured.

These investigation results were shared with an investigator from the FDA's New Jersey District Office during the FDA's recent inspection of the Cherry Hill site. **That FDA inspection, which started on January 17, 2008, was concluded on February 28, 2008 with no inspectional observations (known as Form 483 observations) issued.**

Baxter also tested finished product solutions from "test" and "control" lots. "Control" lots are those where finished product was not associated with adverse reaction reports, while "test" lots were those associated with the cluster of adverse reactions. Samples from both control and test lots were analyzed, using appropriate analytical methodologies, for the presence of potential leachables (container components that have the propensity to migrate into drug solutions and subsequently be introduced into the patient) and trace elements (a chemical element present in minute quantities). The leachables and trace element profiles for the control and test lots were compared, and no meaningful differences were observed.

Baxter has used sophisticated nuclear magnetic resonance (NMR) spectroscopy tests and capillary electrophoresis (CE) tests to identify any differences that might have existed in the chemical composition of the control and test lots. The NMR and CE test results for the test lots showed the presence of extra signals and a peak (respectively, for the NMR and CE tests) that were not present in control lots of the Active Pharmaceutical Ingredient (API), which Baxter purchases from Scientific Protein Laboratories LLC (SPL). Baxter is currently focusing on determining precisely what substance(s) the extra signals/peak represent and what its source might be.

The company now has an indication that the observed differences may be due to the presence of a heparin-like molecule. Baxter is not certain that the differences observed in the API are the source of the allergic reactions. Since the extra signals and a peak are the only significant differences noted between control and test lots of API, **the API is now the focus of Baxter's investigation**.

Baxter has since tested samples of API that were processed at SPL's Wisconsin plant, using Chinese-made crude heparin. Baxter's NMR and CE tests found that four out of five of the Wisconsin processed lots that were most recently tested showed the same extra signals/peak that were seen in earlier tests of lots from SPL's China plant. These results suggest that **the root cause may be associated with the crude heparin, sourced from China, or from the subsequent processing of that product before it reaches Baxter.**

Background on Heparin

Heparin is an anticoagulant that has been used for over 70 years and is one of the most commonly used therapies in the United States. It is administered to millions of patients each year in a wide variety of clinical and surgical settings, and is sold in vial form, pre-filled syringe form, and pre-mixed intravenous bag form. Baxter alone sells approximately 50 million vials of heparin every year. As a commodity pharmaceutical, heparin is relatively inexpensive – most vials sell for less than one dollar.

The potential side effects of heparin have been well known for decades, and are well documented in the literature and product labeling. These side effects include allergic-type reactions.

Heparin, while classified for regulatory purposes as a drug, is in reality a complex biologic, derived from the tissues of living organisms, in this case the intestinal mucosa of pigs. Biologics are by nature more difficult to control and produce in uniform fashion, and demonstrate much more variation in composition than a chemical-based drug.

Baxter produces heparin in "single-dose" vials, which can be used only once, in "multi-dose" vials, which can be used either to draw individual doses for multiple patients or used to create a larger bolus dose for a single patient, and HEP-LOCK "heparin flush," which is used to flush intravenous lines and is much more dilute than therapeutic heparin. Nearly all reported adverse reactions that Baxter has received associated with its recent recall have occurred with our multi-dose vials. Baxter has received some reports of allergic-type reactions with higher dose single-dose vials when single doses were combined to create a larger "bolus" dose. Baxter's single-dose vials, multi-dose vials and HEP-LOCK vials are filled using the same API.

Baxter is one of two of the largest suppliers of heparin products to the U.S. market. **Most of the world's heparin API supply comes from China. Production of API within the United States is insufficient to support the large U.S. market need for heparin products.**

SPL's 30-Year History of Supplying Heparin API

Baxter's supplier of API is Scientific Protein Laboratories, L.L.C. ("SPL") located in Waunakee, Wisconsin. SPL originally supplied API to ESI Lederle, a division of Wyeth that Baxter acquired on December 12, 2002. SPL was first listed as an approved supplier of heparin for ESI in 1972. The only product or service that SPL has ever supplied to Baxter has been heparin sodium API. SPL initially provided heparin API that was refined from crude heparin made from U.S. porcine intestinal tissue and finished in SPL's facility in Wisconsin. In the 1990s, SPL began to explore sourcing the crude heparin from China. **From 1996 to present, SPL has produced regular**

shipments of finished heparin API processed at its Wisconsin facility and sourced from Chinese crude heparin material.

In 1999, SPL created a joint venture with Techpool Bio-Pharma Co., Ltd. called Changzhou-SPL ("SPL-CZ") and later opened a facility for processing crude heparin. This facility was inspected by Wyeth's Global Compliance Division for a qualification audit to ensure the facility met all cGMP (current Good Manufacturing Practice) requirements and the requirements of the business. The SPL-CZ plant successfully completed the qualification audit in 2003.

In February 2004, Baxter submitted a NDA Prior Approval Supplement ("PAS") for use of the SPL-CZ facility as an alternate supplier for heparin API. Baxter's NDA PAS referenced the Drug Master File ("DMF") that SPL had submitted to the FDA for the SPL-CZ facility. The DMF contains proprietary information accessible to the FDA, but not Baxter, regarding SPL's manufacturing process. The FDA approved the PAS in June 2004. The SPL-CZ facility began to process crude heparin for Baxter in November 2004 and has been continuously supplying finished heparin API product with Chinese-sourced crude heparin since that time.

Baxter pays the same price for the API, regardless of which SPL facility Baxter gets the material from, Wisconsin or Changzhou, and the price has remained the same since Baxter acquired the product through the ESI Lederle acquisition in 2002.

Baxter's relationship with SPL is governed by a written supply agreement that requires all API produced to conform to all applicable regulatory approvals, cGMP requirements and all applicable rules and regulations, including the FDA Guide to the Inspection of Bulk Pharmaceutical Chemicals. Other than this contractual supply arrangement, Baxter has no other financial or ownership interest in SPL.

Audits of the SPL-CZ Facility

As noted above, the first audit of the SPL-CZ facility was the full qualification audit performed by Wyeth Global Compliance in December 2002. In September 2003, Baxter conducted a plant inspection, and in November 2004, following FDA approval of the NDA Prior Approval Supplement, Baxter first began receiving lots of heparin API finished in SPL-CZ.

Baxter performed an audit of the SPL-CZ facility on September 20, 2007. This cGMP audit was conducted to verify the effectiveness of the plant's quality systems and technical capabilities. Based on Baxter's review of the SPL-CZ facility, Baxter approved SPL-CZ's continued production of Heparin Sodium USP API pending satisfactory responses to the observations included in the report. SPL-CZ produced satisfactory responses on January 19, 2008.

Based on the successful completion of the audits of the SPL-CZ facility and SPL's Wisconsin facility, Baxter can summarize SPL's performance history with Chinese crude heparin prior to current cluster of adverse reactions as follows:

- Twelve years of successful API manufacturing
- Over 500,000,000 finished doses
- Four FDA inspections/audits
- Five Wyeth/Baxter inspections/audits

Baxter's audit follows the principles of the U.S. Department of Health and Human Services/FDA/CDER/CBER Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients ("Q7A"), an ICH internationally recognized standard.

The Q7A audit process does not apply to the manufacture of raw materials and intermediates further upstream in the supply chain. Baxter relies upon SPL to effectively monitor and audit its suppliers, which is consistent with general industry practice worldwide, both for heparin and other drugs. Baxter (and Wyeth before it) had a positive track record with SPL – including a dozen years of supplying heparin API made with Chinese-source crude heparin and in excess of 500 million of doses of finished product made from that API.

A critical part of Baxter's processes for ensuring that products meet applicable quality standards is the multiple, rigorous testing done on all lots of incoming API and finished products. As a matter of course, Baxter performs more than 15 separate tests on the API and finished product as required by applicable compendia, in this case, United States Pharmacopoeia (USP) standards. USP is the official public standards-setting authority for all prescription and over-the-counter medicines, dietary supplements, and other healthcare products manufactured and sold in the United States. Even though SPL meets USP standards and provides its raw materials to Baxter with the USP designation, Baxter re-tests every lot of the API to ensure that the incoming material meets both USP testing criteria and Baxter's established standards.

When the company's investigation of root cause is complete, Baxter will examine whether the findings suggest that additional requirements ought to be imposed on SPL or other API manufacturers.

Timeline and Update on Recall

At the end of December 2007, as part of Baxter's normal pharmacovigilance process, Baxter noticed an increase in the rate of allergic-type reactions associated with its 1,000 unit/mL 10 mL and 30 mL multi-dose heparin products. The initial reports came from a few dialysis centers. In response to these initial reports, Baxter's quality specialists analyzed the manufacturing and quality control records for the heparin lots associated with the adverse events. **Quality records showed these lots had met all applicable specifications.** Baxter also reviewed manufacturing change controls from January – December 2007, and found no changes to product, process or specifications that could have contributed to these events. Further, all raw materials (actives and excipients) used to manufacture these lots conformed to specifications.

Baxter initiated a manufacturing investigation to determine the most probable cause, and on January 9, 2008, Baxter placed inventory for both the 1,000 unit/mL 10 mL and 30 mL product on hold. On January 8, 2008, Baxter's pharmacovigilance group also began visiting sites where adverse events were reported. On January 11, 2008, Baxter contacted the FDA about these increased adverse drug experience reports at some dialysis centers. The reports all concerned patients that experienced one or more of the following events after administration of a loading dose of heparin for hemodialysis: hypotension, flushing, lips tingling, abdominal pain, chest burning, feeling warm, feeling strange, fainting, diaphoresis, shortness of breath, thirst and nausea. Baxter also told the FDA that an investigation had been initiated to determine the most probable cause.

After January 11th, Baxter received additional complaints against additional lots of Baxter 1,000 unit/mL 10 mL and 30 mL multi-dose heparin. On January 14, 2008 Baxter suspended the manufacturing of its 1,000 unit/mL multi-dose products pending the outcome of an internal investigation. Baxter communicated this additional information to the FDA on January 16, 2008, and also informed the FDA that Baxter was initiating a voluntary recall. On January 17, 2008, Baxter issued a voluntary recall of nine lots of Baxter's 1,000 units multi-dose product.

After this recall was announced, Baxter saw a slight increase in reactions on other lots and sizes of heparin sodium injection beyond the 1,000 units multi-dose vials that had been recalled.

On February 6, 2008 Baxter contacted the FDA to report that the company was contemplating an expanded recall on the multi-dose vials. On February 8, 2008, Baxter reported to the FDA that there had been 348 unique adverse reaction case reports, with 94% of the reports related to 1,000 unit multi-dose vials, 4% of the reports related to the 5,000 unit and 10,000 unit multi-dose vials, and 2% of the reports related to the 5,000 unit single dose vial (8 total). Three of these eight single dose reports concerned situations where multiple single dose vials were used to create a large bolus dose.

Baxter confirmed with the FDA its intent to recall all multi-dose vials in the marketplace on February 8, 2008. However, since Baxter supplies approximately half of the multi-dose vials of heparin used in the United States, the FDA and Baxter were concerned about the supply of heparin in the market if the recall was expanded. After careful consideration, on February 8th, FDA and Baxter concluded that it was better for public health to allow the Baxter multi-dose vials of heparin to remain in distribution so they could be used with caution in situations where the use of heparin was considered medically necessary and alternate sources of heparin were not available. This decision was announced to health care professionals on February 11, 2008 in a broadly disseminated Important Safety Information Bulletin.

On February 19, 2008, there were press reports about APP, the other major supplier of heparin in the U.S. The press reports indicated that APP had increased production of heparin and that APP had the ability to adequately supply the U.S. market with heparin. Baxter immediately assembled information on its own supply situation, including supply that might become available from non-SPL sources. Baxter initiated a conference call with the FDA on February 22nd and discussed whether it could expand its voluntary recall in light of APP's announcement about their ability to supply the market. The FDA (including the Office of Drug Shortage) wanted some time to examine the issue including market supply of all heparin products. On February 27, 2008, Baxter received final clearance from the FDA that it could recall all of its heparin products from the market. Baxter expanded its recall of this product on February 28, 2008 to include all its multi-dose, single dose and HEP-LOCK[1] products.

Investigation of Adverse Event Reports Associated with Heparin

Baxter monitors drug safety surveillance through its pharmacovigilance (i.e., safety surveillance) group. The pharmacovigilance group receives, investigates, analyzes and reports on adverse events. All adverse events must be reported to the FDA either on an expedited or periodic basis, regardless of whether there was any causal relationship between the use of the product and the reported event.[2] **Accordingly, due care must be taken in characterizing the number and types of adverse reactions reported to the FDA and the causal association of those reactions to the drug at issue.**

Since December 15, 2007, Baxter has received approximately 450 reports of adverse events. Of those, we believe that at this time, only four patients suffered an allergic-type reaction to heparin that may have contributed to a fatal adverse outcome. Each of these patients had multiple underlying complex medical conditions and three had either undergone, or was in the process of undergoing, invasive cardiac surgery. These complications make it impossible,

[1] Baxter has not received any reports of adverse events for HEP-LOCK in the current adverse reaction cluster. However, because it is manufactured using the same API as the vial-based therapeutic heparin, Baxter included it in its recall expansion.

[2] Regulatory requirements and pharmacovigilance practice use the term "related" to classify cases where there is a likely causal relationship between an adverse event and a drug, but also in those cases where a lack of information does not allow for the exclusion of a causal link. In other words, a case may be designed as "related" for the purposes of regulatory reporting although there is no data available to actually substantiate a causal relationship between drug and adverse event.

without further medical data, to draw a firm conclusion as to whether these deaths were caused by the allergic reactions. FDA has likewise confirmed that they are aware of four fatalities that have the same clinical characteristics as have been seen with the allergic reactions reporting during this cluster. In addition to these four reports, we have received eight reports where the timing of the heparin administration and the specific medical condition of each patient make it unlikely that these deaths were causally related to the allergic reactions addressed in Baxter's recall. In two further cases, that are the subject of the only litigation so far, no medical professional or family member has provided any medical records or credible information that would allow verification. During the same time frame, Baxter estimates that more than 10,000,000 doses of our heparin product were administered.

The FDA stated last week that they had received 21 reports of deaths from all causes. FDA cautioned very strongly that many of these reports did not contain sufficient information necessary to determine a causal association between the death and heparin from Baxter. This emphatic caution is worthy of careful consideration. As the FDA stated last week, "Just because there's a report in a patient that took heparin doesn't necessarily mean that heparin caused the event. And there are all kinds of events that occur. A lot of these patients are very, very sick." The use, in some press reports, of words such as "linked" or "tied" has created a false impression of a causal relationship when, in fact, the medical facts do not support such a conclusion. For example, the use of the words "linked" or "tied" with respect to the four initial fatality reports that were discussed last month was inappropriate. Our investigation thus far shows that it is unlikely that there is a causal relationship between the allergic reactions and any of these four initially reported patient fatalities.[3]

The difficulty of characterizing a causal relationship is exacerbated in the types of patients who require heparin therapy: patients with end-stage renal disease, clotting tendencies, acute heart attacks, blood clots in the legs or lungs, or patients requiring cardiovascular procedures, including open-heart surgeries. In such an ill and complex population of patients, deaths are unfortunately more likely to occur for reasons having nothing to do with heparin therapy. It would be medically incorrect to assume that, simply because heparin was present at or around the time of death, it played a causal role in the death. Similarly, to indiscriminately ascribe a "link" or "tie" to heparin in these circumstances is inappropriate from a public health perspective, given the critical role heparin therapy plays in saving tens of thousands of patient lives each day.

The second issue impacting Baxter's pharmacovigilance effort is the wide publicity associated with this heparin recall, which has triggered a substantial increase in adverse event reports, many of which lack the substantial medical detail required to determine whether a heparin product was actually involved in the report, if that heparin product was a Baxter product, and what causal relationship between the reported adverse events and heparin, if any, exists. Typically, these reports are being provided by a patient or a relative of a patient who has no medical training and no access to information about the drug the patient actually received, the

[3] In one case, investigation revealed that the patient had not received Baxter heparin. Another case, although reported to Baxter recently, actually occurred in early 2005, almost three years before the increase in adverse reactions that triggered the recall. Additionally, in that case it remains unclear whether the heparin product involved was actually a Baxter heparin product. A third case involved a death as a consequence of bowel obstruction and overwhelming infection, with no evidence of causal association with heparin use. The fourth case involved the death of a cardiac patient in which the role of heparin, if any, was as one of several potential causes of thrombosis, a well-documented side-effect of heparin, and one that is not consistent with the types of adverse reactions reported during the cluster that led to the recall.

manufacturer of that drug, route of administration or formulation. Baxter's efforts to investigate further have been hampered by the unwillingness of clinicians and hospitals to discuss reports, often at the behest of hospital risk managers concerned with malpractice liability after the mischaracterization of the four initial patient deaths as "linked" to the recall.

Moving Forward

Baxter will continue to investigate and analyze these reports to assess whether the reported adverse reactions were causally related to the cluster of allergic reactions that are the subject of the recall, and will continue to forward all reports received to FDA. The root cause investigation is continuing, and our scientists are working collaboratively with FDA and SPL to pinpoint the source or cause of the heparin-like molecule detected in testing to date.

Baxter and FDA have established rigorous quality standards that have been effective for ensuring the safety of heparin for decades and hundreds of millions of doses. In this particular case, those long-standing standards were unable to detect whatever it is that is causing these differences in API. Certainly once more is known about the cause, we will work closely with regulatory authorities and others responsible for developing industry standards to ensure that necessary changes in standards and processes are made.

Testimony of Robert L. Parkinson
Chief Executive Officer, Baxter International
Before Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
U.S. House of Representatives
April 29, 2008

SUMMARY OF MAJOR POINTS

- More than any other company in the world, Baxter's products are involved in critical care settings. Because of this, we are greatly concerned that our heparin product appears to be the target of a deliberate adulteration scheme. Patient safety is our number one priority, and we deeply regret the impact this contamination in Baxter's heparin has had on patients and the clinicians who treat them.
- The developments of the last several weeks have demonstrated that this is both a global and industry-wide crisis, with a root cause – oversulfated chondroitin sulfate ("OSCS") -- that was so novel and so insidious as to avoid the quality systems of a multitude of companies and the oversight of the world's most sophisticated drug regulatory agencies.
- Because of the swift identification of OSCS, and the development of advanced NMR and CE tests methods to detect it, FDA and regulatory authorities around the world have been able to respond proactively, averting a much broader crisis by detecting and screening out the contaminant in other manufacturers' heparin before it was more broadly distributed to patient populations.
- The complexity of the global drug supply chain creates new and emerging risks that call for new ways of thinking about, identifying and addressing vulnerabilities. Resting on old standards – even ones that have worked for decades – is no longer enough. These are the most critical lessons of this entire crisis, and Baxter embraces them.
- We support funding directed to enhancing FDA's ability to fulfill its mission of providing safe and effective products to the American people, and we welcome any opportunity to work with Congress and the Agency in support of this mission.

Testimony of Robert L. Parkinson
Chief Executive Officer, Baxter International
Before Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
U.S. House of Representatives
April 29, 2008

Introduction

Good Morning Mr. Chairman and Members of the Committee. My name is Bob Parkinson, and I am Chairman, Chief Executive Officer and President of Baxter International (Baxter). I appreciate the opportunity to be here today to provide testimony and to respond to the Committee's questions on the crucial topic of medical product safety and the recent recall of heparin products that Baxter and many other companies have implemented.

Our mission at Baxter is to provide life saving and life sustaining medical therapies to patients across the world. We are not a traditional pharmaceutical company. Every one of the products we develop and manufacture is injected, infused or inhaled by patients who need them to stay alive. This is true across our three divisions: our Renal division provides dialysis therapies for patients with end-stage renal disease; our Bioscience division provides biologic therapies for patients with serious blood disorders like hemophilia or primary immune deficiency; and our Medication Delivery division provides a wide range of hospital products for use in acute and critical care settings. If you or a loved one has kidney failure; if your child was born without a functional immune system or with blood that doesn't clot; if you have the misfortune to find yourself in an intensive care unit, an emergency room or an operating room, Baxter products are the difference between life and death. In my four years at Baxter, I have been inspired by the extent to which this is a source of pride for Baxter employees, and it is the source of the profound commitment and responsibility we feel for each of our patients.

Baxter has been in business for over 75 years. More than any other company in the world, our products are involved in critical care settings. Because of this, we are greatly concerned that our heparin product appears to be the target of a deliberate adulteration scheme. Patient safety is our number one priority, and we deeply regret any harm this contamination in Baxter's heparin may have had on patients or impact on the clinicians who treat them.

Through Baxter collaboration with FDA, oversulfated chondroitin sulfate ("OSCS") was identified as a contaminant in certain lots of our injectable vial heparin product. Baxter scientists did not stop there, and in laboratory animal tests have observed a causal relationship between OSCS and hypotensive effects, the results of which were recently confirmed in an article published in The New England Journal of Medicine. Given the knowledge that we have developed over a short period of time, we have made a significant contribution to helping regulatory bodies and manufacturing companies around the world protect the world's heparin supply from this insidious contaminant.

Baxter's Manufacturing of Heparin

Baxter, and its predecessor company ESI Lederle (Wyeth), has been manufacturing heparin in a vial form for over 30 years. Baxter purchases heparin active pharmaceutical ingredient ("API") from Scientific Protein Laboratories ("SPL"), a company located in Waunakee, Wisconsin. Heparin API is derived from the mucosal lining of pig intestines. SPL initially sourced the crude material for its API from the United States. In the mid-1990s, SPL embarked on a program to find other raw material suppliers to assure a consistent quality supply of heparin. Because of supply constraints around the world, SPL, like virtually all heparin API manufacturers, began sourcing this product from raw material suppliers in China, the source of over half of the world's pig supply. ESI and Baxter consistently manufactured heparin made from SPL's API, sourced from China crude, since 1996.

In order to be closer to its Chinese supply chain and to increase its manufacturing capabilities, SPL built a heparin API manufacturing facility in Changzhou, China (SPL-CZ) in 2000. In December 2002, Wyeth Global Compliance performed a qualifying audit of this facility. The facility had run three consecutive validation lots before this inspection. Baxter acquired ESI shortly after this audit. Baxter undertook the process of having SPL-CZ qualified by the FDA as a supplier of heparin API. Baxter submitted a Prior Approval Supplement (PAS) to the FDA on February 6, 2004. The PAS requested that the FDA approve "Changzhou-SPL Co., Ltd. as an alternate supplier" for heparin.

On June 8, 2004 FDA sent a letter to Baxter approving SPL-CZ as an alternate supplier for heparin. Once we received that approval, the manufacture of the API from this facility was approved by the FDA. That approval was not subject to or conditioned on an FDA inspection.

Speaking for Baxter, however: we don't rely on FDA inspections to ensure the quality of our product – that's our job, independent of the FDA's role.

To fulfill this obligation, Baxter relied on Wyeth's December 2002 qualifying audit. In hindsight, we should have conducted our own qualification audit as well, before beginning to receive product in 2004. It bears noting, however, that plant audits were not the only thing we relied on to ensure the quality of our product – we also consistently monitored the quality of both the incoming product we received from SPL and the finished heparin product that we released. Although sample testing is regulatorily acceptable, we tested each and every lot. Our testing exceeded the standards of the U.S. Pharmacopoeia ("USP"), the official public authority that sets standards for all healthcare products sold in the United States. The USP standards for heparin have been successfully used for decades. Unfortunately, we now know that these standards were insufficient to detect this new heparin-like contaminant because OSCS could not be detected with established and validated test procedures. Going forward, Baxter is committed to working with USP and FDA in re-evaluating standard heparin test procedures.

Baxter's Quality team performed a cGMP audit of the SPL-CZ facility in September 2007. The audit consisted of an in-depth review of CZ SPL's quality systems and capabilities including, but not limited to, its supply chain quality systems, such as the documentation and procedures associated with incoming materials and sampling. Baxter was assured that SPL's QA department audits the workshops it uses on an annual basis. SPL also provided assurances that these workshops collect veterinary data for all porcine sources to assure the stock is disease-free prior to collection.

Baxter's Recall of Heparin

Heparin vials are used in a variety of critical care settings, including cardiac and dialysis procedures. Allergic-type reactions are indicated in the label for heparin, and every year Baxter receives approximately 30 reports of adverse events associated with its heparin vial products. At the very end of December 2007 and the beginning of January 2008, we noticed an increase in the rate of reported allergic-type reactions associated with our 1,000 unit/mL multi-dose heparin product, and we launched an investigation. The initial reports came from dialysis centers, so Baxter physicians and quality professionals traveled to reporting dialysis centers. We also began an investigation of our own manufacturing and quality procedures and records for heparin. We also ceased all production and distribution of this heparin product.

After additional adverse event reports came in from other facilities, Baxter (in consultation with FDA) recalled nine lots of its 1,000 unit/mL heparin product that were associated with these adverse events on January 17, 2008. After this recall was announced, we saw a slight increase in reactions in other lots and sizes of heparin. We contacted FDA about expanding the recall. Based on FDA's market data, both we and FDA were concerned about a shortage of heparin. On February 8, 2008 Baxter and FDA concluded that it was better for the public health to allow Baxter's product to remain in distribution so it could be used with caution in situations where the use of heparin was medically necessary and alternate sources of heparin were not available. Baxter sent an Important Safety Information Bulletin to thousands of health care providers on February 11, 2008, apprising them of this situation. When we read that another supplier of heparin said it had the ability to source the U.S. heparin market, we asked FDA for confirmation and, upon receiving it, we expanded our heparin recall on February 28, 2008.

During this recall, Baxter informed health care professionals, customers, renal home care patients, wholesalers, distributors and known customers of wholesalers and distributors by mailing thousands of letters via overnight mail about the recall. Baxter also called thousands of renal home patients directly to discuss the recall. Frequent press releases were issued, a press conference was held, a hotline was staffed and information about the recall was regularly posted on Baxter's website.

Baxter's Investigation of Root Cause

Baxter has been thoroughly investigating the potential cause of the increase in adverse event reports. After multiple variables were ruled out in the manufacturing process and the supply chain, we began to focus on possible issues in the heparin API. Baxter has devoted more than 30 scientists to this investigation and has employed distinguished outside scientists as consultants. Most of our scientists are based at the company's laboratories in Illinois, although we also took advantage of the expertise of Baxter scientists in Europe. We worked openly and diligently in collaboration with FDA on our analytical results. A wide variety of laboratory methodologies and hundreds of different tests were employed in these investigations, including state-of-the-art analytical instrumentation tests such as nuclear magnetic resonance spectroscopy (NMR) and capillary electrophoresis (CE). Using these tests, it was determined that extra signals and a peak were detected in the heparin associated with the recall (test) compared to heparin that

was not associated with the recall (control). The contaminant from the test lots was identified as OSCS.

NMR and CE tests have confirmed that the contaminant found in the API was also found in the crude heparin supply. According to early reports, similar peaks were found in Australia in AstraZeneca's heparin as well as in Germany in RotexMedica's heparin. Neither of these companies received their supply of heparin API from SPL. Since then, the FDA has reported that multiple companies in 11 countries have found this contaminant. Based on the appearance of OSCS in the crude heparin material coming into SPL, and on the fact that other companies with other suppliers have also had OSCS contamination, it is clear that OSCS was added farther up the supply chain, before the crude material reached SPL. Baxter is still trying to understand where exactly the contaminant was introduced.

The introduction of OSCS was difficult to detect because of how closely this contaminant mimicked heparin. Heparin is the most highly charged molecule found naturally in living systems. As such, it is an extremely polar molecule and requires an extremely polar solvent, like water, to stay in solution. In normal heparin production, the heparin is the most polar molecule among the normal constituents of crude heparin (including dermatan sulfate and chondroitin sulfate). OSCS contains more sulfate groups than does heparin, making it more polar than heparin, and making it the first material to lose solubility when ethanol is added to the aqueous solution of impure heparin. Thus, the OSCS is precipitated along with the heparin. In a process designed to collect the most polar material from solution, the OSCS is collected with the heparin.

Over the last few weeks, our investigation has focused on biologic tests aimed at determining whether there is any relationship between OSCS and the increased adverse events that were associated with this recall. The most common adverse event reported was hypotension. Baxter scientists were able to establish that OSCS can cause hypotensive reactions – that is, consistent, prolonged declines in blood pressure – in laboratory animals. They found the same results from exposure to heparin contaminated with OSCS. The hypotensive response was dose-dependent; increased amounts of the OSCS or the contaminated heparin led to greater decreases in blood pressure. Baxter scientists are still searching to understand the cause of a decrease in blood pressure in humans. This result is consistent with the New England Journal of Medicine study in which scientists found a scientific rationale for a potential biologic link between the presence of OSCS and observed clinical adverse events. That article, a copy of which is

attached, reached this conclusion: "Our results provide a scientific rationale for a potential biological link between the presence of OSCS in suspect lots of heparin and the observed clinical adverse events."

Recall of Heparin Around the World

OSCS, the apparent cause of the increase in heparin adverse events, is a very effective imposter that mimics heparin. Not only did this substance avoid detection through long-established USP testing, it avoided detection through the quality systems of several major pharmaceutical companies around the globe, and through the oversight of regulatory authorities in countries around the world, including Australia, Canada, China, Denmark, France, Germany, Italy, Japan, The Netherlands and New Zealand. Because of the swift identification of OSCS and advanced NMR and CE tests methods to detect it, FDA and regulatory authorities around the world have been able to respond proactively, averting a much broader crisis by detecting and screening out the contaminant in other manufacturers' heparin before it was more broadly distributed to patient populations. Baxter continues to cooperate with Ministries of Health around the world and share information we and they have learned about OSCS, including how to detect the presence of OSCS in heparin API and finished product.

Corrective Actions

The developments of the last several weeks have demonstrated that this is both a global and industry-wide crisis, with a root cause that was so novel and so insidious as to avoid the quality systems of a multitude of companies and the oversight of the world's most sophisticated drug regulatory agencies. This extraordinary problem calls for extraordinary corrective actions. It is important to harness the resources and thinking of the entire industry and the global regulatory community to address those new and emerging risks, both deliberate and not, that threaten the safety of life-saving drugs and biologics. In particular:

- Baxter is methodically re-examining our global supply chain practices in light of the heparin mimic that surfaced here, to assess whether unexpected vulnerabilities exist in the supply chain *beyond* our direct suppliers. This review is necessarily going above and beyond current regulatory requirements and industry standards, which proved inadequate to detect this problem. Although less than 1% of all Baxter products sold in the U.S. include components sourced from China, we are beginning our evaluation with a

thorough review of our China-based suppliers and their sources. We have retained recognized experts in supply chain management strategy to assist us in this effort.

- Based on what this full-scale evaluation tells us, we will impose targeted prevention and detection methods on our suppliers to limit exposure to vulnerabilities that exist in their supply chains.
- We have convened a group of Baxter scientists whose mission will be to consider how would-be counterfeiters or saboteurs might threaten our supply chain, much the way that law enforcement or national security agencies have groups dedicated to thinking like potential enemies. By directing outstanding scientific minds at this kind of question, our aspiration is to imagine, address and prevent this kind of threat before it happens. Going forward, we will try to anticipate the unanticipated.
- We believe this type of supply chain threat evaluation is something the FDA and the global regulatory community ought to require more broadly of industry participants. Moreover, we would encourage these agencies to facilitate collaboration on and sharing of these efforts, since the positive changes that could result will be effective only if they are consistently applied and enforced across the industry. Just as the fruits of Baxter's and the FDA's efforts to identify and test for OSCS were immediately shared with the industry in *reaction* to a problem, the world's patients and the global drug and biologic supply would far better served if the fruits of these *proactive* analyses were a common asset for the public good.

Conclusion

Baxter's quality systems for heparin have come under intense scrutiny as a result of this recall. We believe our quality systems are robust, but no quality system is bullet proof. We certainly acknowledge that we should have conducted our own qualification audit of the facility, rather than relying on our predecessor's audit. Importantly, it is not clear that such an additional inspection would have detected or prevented the OCSC contaminant. Therefore, it would be wrong for us to ascribe this problem to a missed inspection and move forward based on improved inspection frequency. Indeed, such a reaction would miss the real points: that the complexity of the global drug supply chain creates new and emerging risks that call for new ways of thinking about, identifying and addressing vulnerabilities, and that resting on old

standards – even ones that have worked for decades – is no longer enough. These are the most critical lessons of this entire crisis, and Baxter embraces them.

Baxter fully supports the allocation of increased resources for FDA. Baxter references the statements by Commissioner von Eschenbach (in testimony last week before this Subcommittee) that FDA lacks adequate resources to conduct effective overseas inspections and to keep a modern and effective database of foreign firms processing products for US patients. We support funding directed to enhancing FDA's ability to fulfill its mission of providing safe and effective products to the American people, and we welcome any opportunity to work with Congress and the Agency in support of this mission.

We appreciate the Committee's interest in medical product safety, and we fully support the Committee's goals. Baxter is eager to continue collaborating with this Committee and others to ensure the safety of heparin. This has been a learning experience for Baxter, and I hope it can be a learning experience for the entire global industry and the global regulatory community so we can all work together to ensure that these types of incidents never happen again. Thank you for giving me the opportunity to be part of this important discussion.

EXHIBIT C

FDA MEDIA BRIEFING ON HEPARIN

Moderator: Julie Zawisza
March 19, 2008
11 a.m. EDT

Coordinator: I would like to thank all participants for holding. All lines will be on listen-only until the question and answer portion of today's conference. I would also like to inform participants today's call is being recorded. If you have objections, you may disconnect at this time.

I am now turning the call over to Julie Zawisza. Thank you. You may begin.

Julie Zawisza: Thank you. Good morning ladies and gentlemen. It is Julie Zawisza here with FDA. I am the assistant commissioner for public affairs. I would like to welcome you to this briefing.

We want to update you on our Heparin investigation this morning. We have some important new developments in the case. So we are going to hear from Dr. Janet Woodcock, who is the director of our Center for Drug Evaluation and Research. And she will provide you with the latest developments. And then we will take your questions.

Dr. Woodcock.

Janet Woodcock: Thank you, Julie.

Well, after weeks of testing and the really (unintelligible), and in some cases, around the clock efforts of scientists, both at FDA and in academic laboratories, the material contaminating lots of Baxter Health Corporation's

blood thinning drug, Heparin, has been identified. The contaminant is an over-sulfated chondroitin sulfate.

Now chondroitin sulfate itself is a biologically-derived compound. It is commonly available.

However, over-sulfated chondroitin sulfate is not ordinarily found in nature. It is most likely that ordinary chondroitin sulfate is chemically modified to create this compound that is found in the contaminant.

Over-sulfated chondroitin sulfate, unlike common chondroitin sulfate mimics Heparin's activities. And therefore appears to be Heparin when it is subjected to standard tests.

Dozens of people were involved in the chemical analysis work to arrive at the identity of this material. FDA labs in Cincinnati, Ohio and St. Louis, Missouri - along with scientists from the Center for Drugs here at White Oak -- partnered with experts from Massachusetts Institute of Technology.

The teams conducted separate tests on Heparin, collected from Heparin active pharmaceutical samples. They also sought input from Washington University in St. Louis.

By conducting multiple different types of testing, the scientists were able to definitively identify the contaminant as over-sulfated chondroitin sulfate.

As we reported previously, the contaminant now identified as over-sulfated chondroitin sulfate was found in many of the samples of Heparin Active Pharmaceutical Ingredient collected from the Changzhou SPL plant in China. This is the plant that supplied Baxter with its Heparin API.

Over-sulfated chondroitin sulfate was also found in some of the Baxter Heparin lots associated with drug adverse reactions.

Analysis of these samples suggests this contaminant accounted for approximately 2 to 50% of the total content of the API in some of these samples.

Over-sulfated chondroitin sulfate is not an approved drug in the U.S., nor should it be present in Heparin, as found by these analyses.

Now that the contaminant has been identified, FDA can move forward to determine how and when in the supply chain this contaminant was introduced.

At the moment, we don't know definitively whether the contaminant was introduced intentionally, or by accident. FDA continues its investigation to track down the root cause of the contamination. And still to be determined is whether or not the over-sulfated chondroitin sulfate, when combined with Heparin, can produce the serious allergic reactions of the sort reported to Baxter and FDA.

We have an intensive immunologic investigation under way to look into the mechanism in how these reactions may have occurred.

The FDA and the U.S. Pharmacopoeia have agreed to collaborate, to develop compendial tests on an expedited basis. The compendial tests will enable Heparin manufacturers in the U.S. and the rest of the world to detect the presence of trace amounts of the over-sulfated chondroitin sulfate.

It is likely these tests will be more rigorous versions of the tests that we have put out in an expedited way for screening.

Dr. Mack Lumpkin, FDA's deputy commissioner for international affairs and special programs, briefed China's State Food and Drug Administration on these findings that I have discussed earlier this week. The Chinese regulators have agreed to assist us in our investigation.

Now, FDA's unraveling of this mystery comes on the one-year anniversary of our discovery of the contaminant melamine in pet food. As in the melamine case, FDA's identification of a highly unlikely contaminant is a result of rigorous and methodical investigation, combined with the use of sophisticated testing.

Also the Memorandum of Agreement with China, which was signed in December, expedited our ability to get inspectors to Chinas to pursue the investigation there, and collect samples with us with no time loss. And this has been a real improvement.

Before opening the phones to your questions, I would also like to bring you up-to-date on other recent developments.

Additional lots of API have tested positive by both SPL and FDA and these lots have been added to SPL's recall.

There may be additional recall information coming out as a consequence of this. These do not affect the large volume of Heparin that is already off the market in the U.S., but may involve other forms of Heparin.

FDA's Office of Regulatory Affairs continues to identify, hold, and examine all shipments of Heparin imported into the country. And will collect samples of those that are of concern. So we are confident that, at the borders, we have a good system in place.

On adverse events, fortunately, since Baxter's expanded recall on February 28, we have received no reports of deaths related to allergic reactions to the Heparin that occurred after that date.

On our last call, there were many questions about deaths and adverse events and when they occurred and so forth. The information is too complicated to present over the phone. And therefore we are going to be posting that on our website for people to look at so that they will have the numbers and the timing of the reports of deaths and when the deaths occurred and so forth.

As was said last time, we feel that doctors and patients now can be confidant that the product on the market for the large volume uses of Heparin - for example, in dialysis and so forth -- has been tested and is safe. However, we do ask that if any adverse events are observed that are serious by doctors or health care professionals, they be reported to the FDA. And information on how to report is on the FDA Web site.

And now I will turn this back to Julie, and thank you.

Julie Zawisza: Thank you Dr. Woodcock. Before we take your questions, I would like to introduce several people from the FDA from around the table here who are also available to answer questions.

And we have Dr. Murray Lumpkin in China who is our deputy commissioner of our Office of International and Special Programs. So thank you very much for dialing at the late hour, Dr. Lumpkin.

We also have Joe Famulare,, who is the deputy director of the Office of Compliance in our Center for Drugs. And we have Dr. Moheb Nasr, who is the director of the office of New Drug Quality and assessment in our Office Center for Drugs. And we have Domenic Veneziano, who is the director of the Division of Import Operations and Policies in FDA's Office of Regulatory Affairs.

Did I miss anyone? I have everyone. OK. Good.

Operator, let's take the first question.

Coordinator: Okay. I would like to inform participants, if you would like to ask a question, press star one on your touch-tone phone. That's star one to ask a question. And our first question comes from Peggy Peck. Peggy, please state your affiliation.

Julie Zawisza: Before we get started, as always, I want to remind folks that we will take one question and then one follow-up, Okay?

Peggy Peck: Yes. Thank you very much. This is Peggy Peck and I want to thank you for taking my question.

Dr. Woodcock, you mentioned that this drug - the over-sulfated chondroitin sulfate is not approved in the United States. Is it approved (unintelligible)? What can you tell us about this drug?

Janet Woodcock: Well, it isn't a drug. It is a chemical compound.

Peggy Peck: A chemical compound.

Janet Woodcock: It is derived. It's is a GAG as we talked about before. It is a member of a family of compounds that are like Heparin. Heparin-like compounds.

It is used in the United States and elsewhere as a dietary supplement. It is biologically derived (unintelligible). It is purified from animals. And, it should not be in Heparin. And it obviously should not be in the form it is in. And I don't know of any intravenous use of such product.

Peggy Peck: So on follow-up, is this the chondroitin this is commonly sold for joint ailments. You see it in health food stores and such?

Janet Woodcock: That is sold as a dietary supplement. Yes, it is in there. It also would be in food. I mean, it is normal body constituent. And, um, yeah.

Peggy Peck: (But) this form, the hyper-sulfated form…

Janet Woodcock: No, the (joint)....

Peggy Peck: That is what I'm trying to find out, this form. About this...

Janet Woodcock: Yes, this form - I'm sorry. I didn't understand. Chondroitin sulfate is, you know, a dietary supplement. The hyper-sulfated chondroitin sulfate would be an experimental compound. It would be something that people have taken to drink, let's say, and sulfanated it - add more sulfate groups to it to change its properties in various ways.

And yes, there are scientific papers about this. There are, you know, various laboratories around the world have done experiments on this - on hyper-sulfating all the different compounds (and seeing) what their activities might be.

Peggy Peck: Is it a most critical experiment?

Janet Woodcock: Not too much. No.

Peggy Peck: Not too much, or not at all?

Janet Woodcock: Not to my - to my knowledge, you know, there certainly isn't as extensive clinical on the biological properties of these hyper sulfated GAGs of different kinds, including chondroitin sulfate.

Julie Zawisza: Next question please.

Peggy Peck: Thank you.

Coordinator: Okay. Our next question comes from Ricardo Alonso-Zaldivar. Please state your company name.

Ricardo Alonso-Zaldivar: Hi. I am with the L.A. Times and thanks for taking my question.

On the last call, Dr. Woodcock, you said that once you identified the compound that it would give you at least some theories as to how it got in there.

Could you, you know, could you bring us up-to-date on what goes on now?

I mean is it the kind of compound that would normally be found in the raw materials from which Heparin is derived. And, you know, would sort of have to be eliminated in the purification process?

Janet Woodcock: No and that's - this compound is not, to our knowledge is not naturally occurring. And therefore,(it would be) easily hyper - or over-sulfated chondroitin sulfate would not be part of something that would be purified away during the purification process.

Ricardo Alonso-Zaldivar: Okay go so that's the gist of it. That it is something that would have been deliberately added in then, right.

Janet Woodcock: We cannot rule in or out whether this is accidentally or deliberately introduced into the product, okay. What we know is that it is something that we are 99% sure is not a natural component that got in there as part of the purification process.

Julie Zawisza: We still have not linked this contaminant to the adverse events.

Janet Woodcock That is correct.

Ricardo Alonso-Zaldivar: But whether accidentally or deliberately added, it would have to be something that was added in?

Janet Woodcock: It didn't come straight from the (pig) if that is what you are asking. So that would be very improbable.

Julie Zawisza: Thank you. Let's take the next question.

Ricardo Alonso-Zaldivar: Thank you.

Coordinator: Our next question comes from Bruce Japsen. Please state your affiliation.

Bruce Japsen: Hi. Thanks for taking the call. Bruce Japsen with the Chicago Tribune.

I think what everyone is going to wonder here is whether indeed this is a counterfeit situation, or a safety situation. I mean we've had other situations where dietary supplements have been passed off as drugs and sent to the United States by counterfeiters.

But how would you describe it to the American people here? What it is that should be a concern. I mean, if indeed this has happened, is this not the first time a foreign substance has been put into, a U.S. pharmaceutical from a U.S. - into the U.S. supply chain?

Janet Woodcock: So you have two questions. One is intent here and then secondly is this the first time a contaminant has been added to a pharmaceutical made outside…

((Crosstalk))

Bruce Japsen: Yeah. And introduced into a U.S. supply chain. I mean, we know that there is certainly, you know, people in their basements or whatever making counterfeit drugs and shipping them to the U.S.

But this is a situation that something was introduced into a drug company's supply chain. Have we ever seen that before?

Janet Woodcock: We are continuing to investigate how this got in, okay. We can't go any further than that, alright. What we are telling you today is that it does not appear to come straight from the (pig). It doesn't appear to be a natural

contaminant that got in there, all right. We do not know how it was introduced or why.

As far as, have their ever been other deliberate adulterations in the drug supply chain? Yes, there have in the past. And that's why we have - we try to have a very strong network of testing and inspections and controls of the drug supply.

Julie Zawisza: Thank you. Let's take the next question.

Coordinator: The next question comes from Heidi Splete. Please state your affiliation.

Heidi Splete: Hi. I am Heidi Splete, Internal Medicine News. Thanks for taking my question.

You said earlier, just reiterating that doctors and patients don't need to be concerned about this. Is there anything further, as far as safety that people ought to know?

Janet Woodcock: Well, I would say, as usual with any medication there are benefits and risks. The medications must be used wisely.

As far as the quality of this medicine, we are doing everything possible to make sure that the quality is tested before it gets out into the U.S. drug supply.

And so, for people who are taking Heparin that has been used in dialysis, or cardiac surgery and so forth, we are sure that these supplies have been tested.

(For all) our uses of Heparin, the testing is going forward on those uses.

So right now, people should not be alarmed. We have not received any more reports, as we said, of fatalities of this type since the recall on February 28.

But we all should always be vigilant, and we always encourage doctors and health professionals to report to the FDA if adverse events are observed.

Heidi Splete: Okay. Thank you.

Julie Zawisza: Next question.

Coordinator: The next question comes from Susan Heavey. Please state your affiliation.

Susan Heavey: Hi. I am with Reuters. Just to go back to where this compound came from. I know Dr. Woodcock has said you don't know (if it didn't come) straight from the pig. Is there a chance it was chemically made and it didn't come from animals at all?

Janet Woodcock: The entire chondroitin sulfate would be chemically synthesized is what you're asking?

Susan Heavey: Right. Instead of animal - instead of derived from an animal. Is that a possibility that you're looking into?

Janet Woodcock: We can't really speculate on that. That would be much more expensive to do that obviously, than simply chemically modify chondroiton sulfate.

Susan Heavey: Thank you.

Julie Zawisza: Next question.

Coordinator: Next question comes from Anna Mathews. Please state your affiliation.

Anna Mathews: I am with the Wall Street Journal.

Julie Zawisza: Anna, could you speak up please?

Anna Mathews: I am with The Wall Street Journal. So it is not yet clear whether this substance is derived - is a chemically-altered version of something derived from animal cartilage, or if was made sort of from scratch.

And do you know if that - if it is from pig cartilage? Because Baxter has said that they believe the substance was from pigs.

Janet Woodcock: We are not able to tell whether it - which animal - what animal it would emanate from at this point in our testing.

Anna Mathews: Are you sure it does emanate from an animal? Or you are not sure of that either?

Janet Woodcock: As I said, synthesis from scratch of this would be very expensive. Is that Dr. - I will ask Dr. Nasr to comment on that.

Moheb Nasr: Yeah, this is Moheb Nasr.

I think we can say the following: that over-sulfated chondroitin sulfate was chemically made by modifying the existing and abundant chondroitin sulfate that comes from a variety of animal sources.

Anna Mathews: From cartilage?

Janet Woodcock: Yes, it is ordinarily purified from animal cartilage.

Moheb Nasr: Yes.

Julie Zawisza: Thank you. Next question please.

Anna Mathews: Thank you.

Coordinator: Next question comes from Brian Hartman. Please state your affiliation.

Brian Hartman: I am with ABC news. I am just wondering if you have any idea, you know, with the (pet food) we all are obviously thinking about the pet food and melamine when we think about this.

Is over-sulfanated chondroitin sulfate, is this something that is cheaper - much cheaper than Heparin to produce? I would assume it is, right.

Janet Woodcock: Well, the base compound chondroitin sulfate is a very abundant and inexpensive compound.

Julie Zawisza: Is that it, Brian?

Brian Hartman: That's all. Thanks.

Julie Zawisza: Next question.

Coordinator: The next question is from Marc Kaufman. Please state your affiliation.

Marc Kaufman: I'm with the Washington Post. And it was said...

Julie Zawisza: Marc?

Marc Kaufman: …it was asked earlier if this at this point with be - could be determined to be counterfeit.

Julie Zawisza: Marc, we are having trouble hearing you.

Marc Kaufman: Okay. Can you hear me now?

Julie Zawisza: We're having some technical issues, but...try again.

Marc Kaufman: Okay.

Julie Zawisza: I don't hear you at all.

Marc Kaufman: Can you hear me better?

Julie Zawisza: Yes. Thank you.

Marc Kaufman: Okay. You had said - someone had asked earlier whether or not if this was to be declared to be a counterfeit. And (unintelligible) that question was specifically answered. So I was wondering if you could tell us whether or not you think that would be an accurate description at this point.

And as a related thing, if it turns out that this is counterfeit, and was either intentionally or unintentionally put in there, what kind of authority does the FDA have to respond in a foreign country?

If this was in the United States, obviously there could be criminal penalties. Could there be such things in foreign countries?

Janet Woodcock: This is Janet Woodcock. I will turn this over to Joe Famulare from our office of compliance in a minute.

But the counterfeit (unintelligible) can be a little confusing, because we don't know how this got in there. There is Heparin in this product, all right. However, it is contaminated or adulterated with this other over-sulfated chondroitin sulfate. So that's the status of it right now.

Joe Famulare: I think that is accurate, what Janet Woodcock said. Right now we are looking at it as an added material, or a contaminant, or an adulterant that should not be there, so I think it is premature to use that other terminology at this point of our investigation.

As far as, you know, as far as our authority in another country, I think as Dr. Woodcock pointed out, we are working with the Chinese authorities to work through this investigation. It is open right now. And we will be able to - particularly with the benefits we have, using the MOA, work through these issues.

We have done them in the past. And as you correctly point out, there's a difference than if we were doing it here in the United States. But we can use various cooperations to further the investigation.

Julie Zawisza: That was Joe Famulare in our Office of Compliance. Dr. Lumpkin did you have any further remarks? Or Dr. Woodcock?

Murray Lumpkin: No, I think Joe handled it fine. Thank you.

Julie Zawisza: You're welcome. Okay, anything further? Okay. Next question please.

Coordinator: The next question comes from Drew Armstrong. Please state your affiliation.

Drew Armstrong: Yeah, I am with Congressional Quarterly. Actually I had a question for (Joe). Again, I am wondering if you could characterize the cooperation by the Chinese government and their regulators there.

Have they been very cooperative, somewhat cooperative? Could you go into a little bit of detail and the attitude there?

(Joe Samulari): I think we should go primarily to Dr. Lumpkin, who is right there on the ground level.

Drew Armstrong: Oh, yeah. My mistake. Thanks.

Julie Zawisza: Dr. Lumpkin.

Murray Lumpkin: Yes, that is no problem. I would characterize it as very cooperative on this. And as Dr. Woodcock said, it is quite a different scenario than we had a year ago with melamine. Some of the specific examples, the Chinese government was extremely quick in doing the Visas when we asked for them to help get our inspectors into China as quickly as possible.

And inspectors from the state's Food and Drug Administration here in Beijing accompanied our inspectors during the time they were here in China.

I have been in China this week. I was supposed to have been here anyway, but because I have been here, I have been in contact with our counterparts here at the State Food and Drug Administration. They have been extremely helpful and interested in our data and in sharing what they have been doing with us.

Julie Zawisza: Thank you, Dr. Lumpkin. Let's go to the next caller.

Coordinator: The next question comes from Elizabeth Weiss. Your line is open. Please state your affiliation.

Julie Zawisza: Beth?

Coordinator: Elizabeth, your line is open. Check your mute button.

Julie Zawisza: How many more people are on the line, Operator?

Coordinator: How many more questions?

Julie Zawisza: Yeah, queued up.

Coordinator: About seven more questions queued up at this time.

Julie Zawisza: We will do our best. I am not sure if we can get through all of them, but we will try. If Elizabeth Weiss comes back, could you put her in?

Coordinator: Sure. And our next question comes from... Okay. Our next one comes from Anna Edney. Please state your affiliation.

Anna Edney: Hi. I am with Congress Daily. Dr. Woodcock. I just wanted to clarify. I think you sort of went over this. But you mentioned that modifying the chondroitin sulfate is expensive.

Is it more expensive than manufacturing the API?

Janet Woodcock: No, what - I don't - I you are asking if you could make chondroitin sulfate from scratch? In other words, not get it from an animal, but synthesize it from scratch. And I said that would be expensive. Modifying it or sulfanating it would not be that - I'll ask - I'll refer that to Dr. Nasr.

Moheb Nasr: Yeah this is Moheb Nasr.

Chondroitin sulfate by itself is certainly not expensive. It is abundant and cheap. We are defining it by making it over-sulfated chondroitin sulfate would not be that expensive either.

Julie Zawisza: Next question.

Coordinator: Next question comes from (Kate Trainor). Please state your affiliation

(Kate Trainor): Hi, I am with the American Journal of Health System Pharmacy.

This has been partly addressed. Dr. Woodcock has said that the large volume usage of Heparin, all the products have been tested and found safe.

So you are working on other products? Are you referring to Heplock Flush Solution? And how did you go about getting confirmation from the manufacturer that they have been tested?

Janet Woodcock: What we are doing is, you know, in our investigation is looking at the API sources of Heparin, okay, because those go into all these different distributed products. You know, it might be a small amount of Heparin in this or that or the other thing.

To our knowledge, we haven't had any adverse events reported unusually with this - with these types of devices and so forth that have small volumes of Heparin.

However, our strategy is to go to the source where the API - the source of Heparin – and test that. Because that would then be distributed out to, you know, various other manufacturers to use. So that's the strategy we are pursuing and we are pursuing that very aggressively.

(Kate Trainor): Okay, how much more testing do you think remains to be done of Heparin out there right now in the U.S.?

Joe Famulare: This is Joe Famulare. We have a regular program of testing - both within FDA and with companies that have already agreed to do testing as part of their screening before using the API in manufacturing their product. So that will go on as we continue on to develop more robust methods that Dr. Woodcock mentioned in her preliminary remarks.

And so that companies will be testing. And we will correlate that with (unintelligible) folks in ORA. As, Dr. Woodcock mentioned, that will be looking to sample at the border where we don't have any evidence of testing and clearing any particular material coming in.

Julie Zawisza: Thank you. Next question.

Coordinator: Next question, Justin Blum. Please state your affiliation.

Justin Blum: Hi. This is Justin Blum with Bloomberg News. Thanks for taking the call.

There is one thing you said, Dr. Woodcock, that seems like it could be a contradiction. Which is that, the substance, chondroitin sulfate, was intentionally modified. Yet at the same time you are saying you don't know if it was intentionally introduced.

If it wasn't intentionally introduced, why would it have been intentionally modified and added?

Janet Woodcock: As I said, people are experimenting with these different GAGs to make other - make products and chemicals and so forth. It is possible this could have accidentally contaminated a (unintelligible). But we do believe it was chemically modified.

Justin Blum: Okay. And then a follow-up question, which is I know you've touched on the cost issue before. But do you have a sense of how much cheaper it might be to substitute this contaminant for the equivalent amount of the actual raw Heparin?

Janet Woodcock: No. We don't have any quantification on that.

Justin Blum: But it would be cheaper?

Moheb Nasr: Yes.

Julie Zawisza: That was Dr.?

Janet Woodcock: Yes.

Julie Zawisza: Nassar.

Janet Woodcock: It obviously depends on market conditions for all the different ingredients. So we don't - w can't give you any numbers.

Justin Blum: Okay.

Janet Woodcock: That is somewhat beyond our scope anyway.

Julie Zawisza: Exactly.

Janet Woodcock: (Unintelligible) beyond the scientific investigation.

Julie Zawisza: Next question please.

Coordinator: Next question, Walt Bogdanich. Please state your affiliation.

Walt Bogdanich: New York Times. Since it is cheaper to make than regular Heparin, is it your operating hypotheses that it was most likely counterfeit?

I mean, you certainly have some inclination at this point as to what - whether it was intentionally added or not, based on the fact that it is less expensive.

Janet Woodcock: Well, as I said in my opening remarks, we don't have any evidence, one way or another whether it was accidentally or intentionally introduced. There is a very broad investigation and very active investigation going on and that's all we can say about that.

Walt Boganich: Okay.

Julie Zawisza: Thanks, Walt. And we will take one final question this morning.

Coordinator: Okay. Last question, Rob Foreman. Please state your affiliation.

Rob Foreman: Yes, I am with the CBS Early Show. And I believe the last two questioners, stole my thunder. So if anyone else has one, please move on. I would be very interested in whether there is any profit in, you know, what they would say, the bar watering the stuff down.

Julie Zawisza: We don't have that information at this time.

Coordinator: Okay. We will take one more then from Daniel Poppy. Your line is open.

Daniel Poppy: Hi. Thanks. Can you say a little bit more about how the MOA has helped (expediate) the investigation? You sort of said a little bit about it, but can you provide more detail?

Julie Zawisza: Dr. Lumpkin, are you still with us?

Murray Lumpkin: I am. I think the - it (unintelligible) done in several ways. The example that I mentioned first about the ability to get the Visas to get our inspectors in was one that helped us get the samples as quickly as possible.

I think we have also had ongoing discussions with our Chinese colleagues, as the investigation has progressed.

This is the kind of relationship that did not exist during the time of melamine about a year ago. We continue to work with our Chinese colleagues, and they have stated many times that they will continue to work with us on this, until we find out what happened here and who was responsible for what happened.

Daniel Poppy: And one follow-up. Is there talk of adding Heparin to the designated API list, that is done annually?

Murray Lumpkin: You know, I think that is a very interesting question. Actually, the discussions that we have had, Heparin has become kind of an example of how the MOA actually works in a real live situation, as opposed to having to look at the designated products.

So we decided adding it or not adding this to the list is really rather immaterial. It is indeed the living example of the MOA working.

Daniel Poppy: Thanks.

Julie Zawisza: Thank you. With that, we will conclude this briefing this morning. And I would like to thank all of you for joining us. And thank you to our speakers, Dr. Woodcock, Dr. Nasr, Joe Famulare, Dr. Lumpkin, Domenic Veneziano.

If you have follow-up questions, please call Heidi Rebello in the press office at 301-827-6243. If you would like to listen to this briefing on the instant replay, here are the numbers. Toll-free: 800-843-4802. International callers, 203-369-3835.

And as Dr. Woodcock mentioned, please check our web site today. I think today, right.

((Crosstalk))

Julie Zawisza: We hope to have today updated information on the adverse events - timing of the events themselves and when they were reported to the FDA.

There is a lot of work going on here behind the scenes, as you have heard. So we promise to keep you updated. As we can make information public, we promise to do that. And with thank you again for participating. And you have a pleasant day.

END

EXHIBIT D

FDA MEDIA BRIEFING ON HEPARIN

Moderator: Karen Riley
April 21, 2008
2:30 p.m. CT

Coordinator: Good afternoon and thanks for standing by. At this time all participants are in a listen only mode. After the presentation we will conduct a question and answer session.

Today's conference is being recorded, if you have any objections you may disconnect at this time.

Now I would like to introduce your host for today's conference Miss Karen Riley with the Office of Public Affairs with the FDA. You may begin.

Karen Riley: Thank you. Welcome to today's media call. We're here today to provide you with an update on FDA's ongoing heparin investigation. With me on the call today is Dr. Janet Woodcock, director of FDA Center for Drug Evaluation and Research.

She will provide an opening statement then we will go to Qs and As. Before we start today's discussion let me remind people that today's call is for credentialed media only.

So, we have a lot to say and so let's get started. Dr. Woodcock.

Janet Woodcock: Thank you. The purpose of this call is to update you on the progress of our work on the problem of heparin contaminated with oversulfated chondroitin sulfate or as we call it OSCS that has been associated with serious adverse events.

As you know because there is no routine method to test for this contaminant, FDA developed analytical methods for testing heparin active pharmaceutical ingredients which we've posted on our website on March 6th.

On March 12th we followed up with a request that US manufacturers and suppliers test all lots of heparin API. We encouraged regulators worldwide to check their supplies with these new test methodologies and provide a contact for regulators and manufacturers to update us on their results.

Many regulators and manufacturers have done so. What we've found is that contamination of the heparin supply is a worldwide problem. Contaminated heparin has now been found in some lots of heparin in at least ten [plus U.S.] countries, and we're posting a map that will show which country - in which countries this has been found.

These findings of contamination are leading to quarantines and ongoing recalls of the affected products in many parts of the world. The contamination has been detected in API lots that were manufactured at least as early as 2006.

Because of the time frame for manufacturing final heparin dosage forms from API, the contaminated heparin generally entered the worldwide market in 2007.

It found its way into drug products, IV flush products, medical devices, and possibly in vitro diagnostic tests. All of these products are being tracked down and evaluated by regulators and manufacturers.

At the present time to our knowledge, adverse events have been reported only when patients received a large bolus dose intravenously. We do not know where the contamination occurred.

However we do know that the contaminated products used product from API and crude heparin companies across a broad area of China. Additionally we now know of at least ten Chinese firms that are in the supply chain for contaminated heparin.

We also requested manufacturers of another form of heparin, low molecular weight or fractionated heparin, to test their products and API. That's because they use heparin as the source of low molecular weight heparin.

Testing of these products by various manufacturers has also revealed some contamination by oversulfated chondroitin sulfate. Regulators in various countries are evaluating the low molecular weight heparin situation in their area. And we discussed this at the regulator's meeting that I'm going to talk about in a minute and arrived at a consensus about the approaches.

Low molecular weight heparin is generally used for a short period of time for blood thinning or anti-coagulation to prevent blood clots from forming in the veins or preventing extension of blood clots that are already formed.

I'd like to stress for US health care practitioners and patients that fractionated heparin currently on the US market with a trade name of Lovenox and others has been tested and is free of contaminant.

We will continue to provide to you complete information on the status of heparin supplies in the US.

Because of the scope of this problem that was revealed by the testing, FDA held a meeting on April 17th and 18th with international regulators representing more than ten countries.

The Chinese SFDA and Chinese scientists attended. The USP and the European pharmacopeias participated and we also had several academic heparin experts.

The goals of the meeting were to discuss the analytical testing results related to the worldwide heparin supply and to share inspectional issues and findings.

Now we had two days of meetings but a brief summary is that the testing discussion revealed that we found only one contaminant, something that should have been there was identified in the samples tested and that was the oversulfated chondroitin sulfate.

So that was identified as - it was the same contaminant. The proton NMR and the CE methods posted by FDA were successfully used around the world.

The analytical scientist identified a need for more well-developed screening methods and confirmatory and quantitative methods generally.

And that means we need a screening method that is easy to use and can be put into place routinely, and also, if we find anything, we need methods where we can then identify and find out how much is there.

There was agreement on the need to update the compendial testing method. These are for example what the USP uses and others that is required for heparin to be tested.

USP and the European pharmacopeias have agreed to collaborate to rapidly incorporate testing relevant to oversulfated chondroitin sulfate in the short term but also to develop more comprehensive methods for demonstrating purity over the long term.

So these methods will be modernized. Testing also revealed in some of the samples an excess level of a known heparin impurity, dermatan sulfate in a number of samples.

Because of this it was agreed there should be a public standard for dermatan sulfate content. As you know heparin is derived from the intestines of pigs and dermatan sulfate is a byproduct of this process.

But the amount of dermatan sulfate in some of the samples was in excess of what we would expect significantly for a byproduct.

Also in the regulator's meeting there was a discussion of the low molecular weight heparin findings and as I said general agreement on how to approach low molecular weight heparin.

For the - we also had inspectional discussions about the inspectional results. We agreed - we have an international rapid alert notification system, and this has worked very well in this crisis.

And the international regulators agreed to utilize and enhance this notification system. The heparin problem generally illustrated the need for us to focus on enhanced regulation and scrutiny of the whole supply chain for drugs, including all sources of materials, including the natural sources.

And the regulators agreed to hold an inspection summit in 2009 to apply lessons learned from the heparin situation, particularly on how regulators worldwide can continue to build on existing collaboration.

The Therapeutic Goods Administration of Australia or TGA will lead the organization of the summit and FDA will host the summit.

And the list of invitees to this inspection summit will be much broader than the folks who were at the heparin focus meeting.

So in summary of that part, about the inspection issues, we felt there have been excellent ongoing cooperation and the meeting helped to exchange knowledge on the ongoing investigation amongst the regulators that will continue - that we will continue to collaborate on that.

In addition, at the meeting the Chinese scientists noted that China has instituted testing of [heparin] API prior to export. API's testing positive for OSCS contaminant will not be given a certificate of analysis and will not be exported from China and that is what we were assured by our Chinese colleagues.

Now to move to a different issue, as you know FDA has been conducting an investigation into the biological link between the OSCS contaminant and the observed adverse reaction.

We have very recently evaluated data that we feel provides a very solid mechanistic link between the adverse reactions observed after bolus dosing and the OSCS.

We plan to publish these data very expeditiously so they may be evaluated by the scientific community. It's very important we all be confident that we understand the link to ensure that the testing that FDA and others have put into place will prevent further adverse reaction.

We are aware that our Chinese colleagues are skeptical that such a link has been established. Therefore we are hoping to have further scientific dialogue with them within the next few weeks to present the data as we work together with them to resolve this complex situation.

Finally, our website contains updated information on heparin adverse events, I stress that as you know the occurrence of an adverse event in a patient taking a drug does not mean that the drug caused the problem.

With the heparin situation, the pattern of reports is the most powerful indicator. What caught our attention in heparin was the rapid increase in the number of deaths reported after heparin administration.

We now know there was an increase in November 2007 that persisted through February 2008 and returned to baseline in March and this coincided with our identification of the problem and the recalls.

That concludes our update, and I'll turn it back to Karen for questions.

Karen Riley: Thank you. There are a couple of other things I'd like to point out. Number one, we do have a new warning letter, Changzhou SPL warning letter and we can provide the links to all reporters who would like that link.

And secondly in addition to posting a fresh adverse event data we also have posted a map on the heparin website that illustrates you know where heparin,

contaminated heparin has been found in the world, the ten countries where this has been identified.

Okay, before we go to the phones for question and answers, again let me remind you that this call is for credentialed media only. We have a very crowded phone line so we can only take one question and one follow up question from each reporter.

And we do have some experts standing by to answer questions, should technical experts in case we need to call on them. So with that let's go to the phones for questions.

Coordinator: If you would like to ask a question, please press star 1. Please identify your affiliation when asking you question. To withdraw your question, please press star 2.

Once again, if you would like to ask a question please press star 1. The first question is from Peggy Peck, your line is open.

Peggy Peck: Yes, hello, thank you for taking our questions. My first question is this - I just would like to clarify what you're saying about establishing this link. Are you saying - if I'm understanding you correctly, you are confirming that it is the contaminant that caused these adverse events?

Janet Woodcock: What we're saying, this is Janet Woodcock we have data in vitro, in a test tube in other words, as well as animal data that shows that this contaminant can trigger events that would lead to these type of reactions, that's right.

That doesn't tell us everything of the whole story, but it establishes a link. And we hope to publish these data very rapidly.

Peggy Peck: Okay, and on follow - my follow up question is that do you have any additional data on these comments made by the commissioner in his testimony last week about the motivation behind the contamination of the heparin?

Janet Woodcock: No.

Karen Riley: Okay, we'll go to the next question then.

Coordinator: The next question is from Justin Blum, your line is open.

Justin Blum: Hi, thanks for taking my question, I have a question and a follow up, first you posted on the website a map showing eleven countries where heparin contamination is present.

You said there were ten countries and below the map it says ten countries have reported the presence, but which country shouldn't be highlighted in the map or should it really be eleven countries?

Janet Woodcock: We probably weren't counting the US.

Justin Blum: Okay. And the follow up question is that the Chinese are arguing that over oversulfated chondroitin sulfate couldn't be the cause of the deaths because it's been found in other countries where it hasn't lead to deaths and adverse reactions.

So they say there must be something unique about Baxter's product if it's lead to deaths and adverse reactions while these other company's products haven't.

Can you explain why you disagree with that assessment?

Janet Woodcock: Well we have seen a significant cluster of similar events in Germany as you know in dialysis patients number one. But the root of administration and the bolus administration may be related to why we saw the adverse events we did.

Certainly even in the US the adverse events did not occur in every individual who was exposed to this. So there's some biologic variation.

But we discussed this with the international regulators and it does appear that the root of administration and perhaps the amount that's administered and how fast it's administered may play a role.

Justin Blum: And if I could on this map as I look at it again where you list the countries at the bottom, the supposed ten countries, the United States is not included on the list.

The map has Japan highlighted but Japan is not included at the list at the bottom of countries. So are you saying that there was contaminated API found in Japan or no?

Karen Riley: Justin, no lies, we will circle back and fix the chart.

We'll check our fingers. We have - I just checked, there are definitely eleven countries, we left out the United States because we didn't identify the United States on the map since most people would know that that was the United States.

So we will fix that, there were eleven countries and all the other countries that are on that list were contaminated.

And you are by the way with Bloomberg News. Please identify your organization when you ask your question. Next question please.

Coordinator: The next question is from Elizabeth Weise, your line is open.

Elizabeth Weise: Hi, thanks for taking my call, Elizabeth Weise with USA Today. I'm wondering if you can run over the mechanism whereby you believe that this contaminant is actually causing this allergic reaction.

Janet Woodcock: We - it would be getting too deep into the technical weave, okay, to go over in detail, that's why we published it.

However, we think just a mediator reaction that the oversulfated chondroitin sulfate when it's rapidly injected in the blood, triggers mediators that can cause this reaction.

Elizabeth Weise: So that's why it's got to be a larger bolus to actually have this effect.

Janet Woodcock: Well our data indicates that there is a dose response on there. It's not what you think of as classically as allergy.

Elizabeth Weise: Okay.

Karen Riley: Okay, thank you, next question please.

Coordinator: The next question is from Bruce Jepsen, your line is open.

Bruce Jepsen: Thanks for taking my call, Bruce Jepsen with the Chicago Tribune. I wanted to follow up just sort of a broad question.

So relative to whether you have a root cause and you've established the - you know whether the causality, the intention, you know what people's intentions were in putting this in there and also is this an animal-like substance?

You said that the sulfate, it's the same thing that was found everywhere, and then you also mentioned like these ten Chinese companies, I'm a little confused here.

Because if you're saying it's the same thing found in you know all around the world, what was it? I mean what was it and how did it get in there and what are the ten companies and were they all Chinese? I'm a little confused.

Janet Woodcock: Yes, there - to answer your last question, these are ten different Chinese companies that have been shipping API or involved in heparin manufacture where we've been able to trace back at least one lot of contaminated heparin as originating there.

Karen Riley: Does Deb Autor want to get on the call on this?

Janet Woodcock: So yeah, I'll let Deb answer, let me just finish answering the first part of your question. What we're saying, we got all the analysts around the world together who have been running these tests, okay.

And we were able to determine by all of them sharing their message and you know tests and everything that they're finding the same compound. And this compound is as we said earlier, we believe it is artificial.

In other words, it is a modified naturally occurring product that has been chemically modified. And in its modified form it mimics the biological activity of heparin.

Bruce Jepsen: But for the you know little old lady in Wilmette Illinois who doesn't know what the heck chondroitin sulfate is, I mean you had said before that this comes from like you know cow bones or something, I don't know, you know what I'm saying?

You're saying it's all the same which are around the world. So break it down for me please.

Janet Woodcock: Okay, all right.

Bruce Jepsen: And also on these ten different Chinese companies, I mean are these like big pharmaceutical companies, are they - what are they?

Janet Woodcock: All right, okay. For the - basically what we're saying is that there was something in heparin that there shouldn't have been, right?

And it's - and when we tested around the world we found that different lots of heparin all over the world have this in it and it's the same compound. Yes, it is something that could be made from animal sources and then chemically modified, all right?

So that's the first part, you'll have to be in charge of the little lady in Peoria.

Bruce Jepsen: Well ma'am,. Nobody in Peoria reads us any more.

Janet Woodcock: Okay, I'm sorry to hear that.

Bruce Jepsen: I'm kidding, I'm kidding.

Janet Woodcock: And then what was your second question?

Bruce Jepsen: About the ten - describe for me the companies, I mean are these like the Chinese version of you know big companies, are they warehouses, are they…

Janet Woodcock: Deb Autor who's the head of compliance in the Center for Drugs will describe that for you.

Deborah Autor: Yeah, there are - we've actually said at least ten, so there's actually a total of twelve Chinese companies in the supply chain for the contaminated heparin and they are located in various locations throughout China.

And they've supplied either crude heparin or heparin API. I don't have in front of me data on the size of them, I would think it's fair to say they're not all large companies.

Bruce Jepsen: What do you mean by how large, and I don't mean to dominate this but I'm hoping people will weigh in.

Deborah Autor: Yeah, I don't have that information exactly in front of me, I think that there are…

Bruce Jepsen: Five employees, a shack on a farm, or…

Deborah Autor: I don't have those data.

Janet Woodcock: Right, to be clear though, they're not making the final dosage form, they're not making the vial or whatever that ends up in the hospital.

They're supplying the heparin material that's been shipped elsewhere around the world to be made into a final form of some kind.

Deborah Autor: I probably used the term API which is the active pharmaceutical ingredient.

Karen Riley: Okay, are you all clear? Next question please.

Coordinator: The next question is from Gardiner Harris, your line is open.

Gardiner Harris: Thanks for taking my call, it's Gardiner Harris with the New York Times. I guess just to follow up with Bruce and the other question, is there some sense that each one of these ten companies was doing something that then got this contaminant in there?

Or are some of these ten or twelve companies then simply a little bit further down the stream?

Do you know - and one other sort of question and that is in discussions with Chinese officials, they - I asked them about whether they are going to allow FDA to open three offices in China as Dr. (unintelligible) said and they have said, 'Well we're in discussion about whether that offer is reciprocal and whether we need to open office in the United States.'

Can you tell me the state of your cooperation with FDA and China, you all have said previously that it's very good and improving, these sort of latest test methods would suggest to me that things are not so great.

Janet Woodcock: Are international affairs on the phone? Do we have someone from international affairs?

Deborah Autor: Let me answer the first part while you're working on that which is that we do not know at what point in the supply chain the contaminant may have been introduced, so we are not saying that necessarily each of these twelve companies introduce a contaminant to the product.

We simply said that there are twelve different Chinese companies in the supply chain for contaminated heparin.

And I think Dr. Woodcock talked about the fact that we are hoping to have further discussions, scientific discussions with the Chinese within a couple of weeks.

We understand that they want to learn more about our thinking on the scientific issues. They were able to come to the international meeting and work with us through that meeting to talk about a lot of the issues presented.

And they are also - we understand taking extra measures in China to regulate heparin and to make sure that heparin API, excuse me, active pharmaceutical ingredient is screened for potential contamination before it leaves China.

So I think there are a lot of positive signs on the horizon.

Gardiner Harris: Thanks.

Karen Riley: Great, thank you, next question.

Coordinator: Your next question is from Susan Heavey, your line is open.

Susan Heavey: Hi, in addition to the map that was put on line there's also a new table with new numbers on the deaths and allergic reaction. Before the FDA had said that they had 62 deaths that were linked to these reactions.

Is that new number now 81?

Karen Riley: That's correct.

Janet Woodcock: Yes, the - we aren't saying they're linked, we're simply saying as you know that the pattern shows that there was an increase during those months which has now gone down to baseline.

But as we have repeatedly pointed out, just because somebody got heparin and they had a reaction, it doesn't imply a causal relationship and there's always been some background incidents in these reactions reported.

Susan Heavey: And can you tell me how many of those 81 are linked to Baxter's products?

Janet Woodcock: No, these keep coming in so we have to go through a lot of them - often do not have the manufacturer's number. So at some point we will post more information on that when we're sure.

But it's that we have to follow up on all of that.

Karen Riley: Susan, I would remind you that also if you look at the month by month tally that the trend continues, that it really started in about November and it ended in about February.

Susan Heavey: Okay, thanks.

Karen Riley: Next question please.

Coordinator: The next question is from Ricardo Zaldivar, your line is open.

Ricardo Alonso-Zaldivar: Yeah, Ricardo Alonso-Zaldivar with the LA Times, thanks for taking my question.

I just wanted to ask you, other than Germany, have any other countries reported adverse reactions to the heparin? Is it only a problem with Germany and the United States?

Janet Woodcock: Yes, we have talked to all the other regulators, they have not seen increases in adverse events.

Ricardo Alonso-Zaldivar: Okay, and to follow up then, what would explain that? Doesn't that seem to strengthen the argument of the Chinese regulators that there must be something else other than this contaminant?

Janet Woodcock: Well as I pointed out, there are many people in the United States who got this who did not get an adverse event to it. And we did speak to for example some people in Europe do not use bolus dosing of heparin very often.

So we are not able to rule out the fact that there, that there could be the other problems leading to these adverse events but the fact that we've now established a mechanism by which we think this contaminant could cause these adverse events, we think strengthens the association considerably.

Ricardo Alonso-Zaldivar: Okay, and follow up on that just a second, could you explain a little bit more about the mediator reaction that you mentioned earlier?

Janet Woodcock: Sure, what we're talking about here is that looking at in the test tube if you use contaminated heparin or synthetic material, this OSCS, you can see changes in what are called blood mediators that could lead to this reaction.

In addition, these have been observed in animals. And we have emerging data, we just heard about today from another source, another group of experimenters who have also observed this.

So we think this story is starting to come together.

Karen Riley: Thank you, next question please.

Coordinator: The next question is from Alicia Mundy, your line is open.

Alicia Mundy: Hi, it's Alicia Mundy from the Wall Street Journal and thank you for taking my question.

I had just a question about the different ways that the Chinese and the United States FDA and pharmaceutical testing labs are screening for the contaminant.

Is - are the Chinese using the same kind of detection methods we are and if not are those detection methods and screening tests available to them?

Janet Woodcock: I'm not - we're not sure exactly everything that the Chinese are using or what they have available, but I think we're putting measures in place in multiple parts of the supply chain.

So the Chinese will be testing before the heparin leaves their country, but our manufacturers will be testing before they would put an API into a finished dosage form.

So there's going to be multiple steps of testing instituted. Dr. Moheb Nasr may wish to comment on this more extensively.

Moheb Nasr: Yes, this is Moheb Nasr. An analytical method [capillary electrophoresist] that was put in place, and we published last month has been used by all the regulatorial authorities around the world.

And they have concern that the value and they were able to identify the same contaminant oversulfated chondroitin sulfate. Our Chinese colleagues in addition to (unintelligible) methods have used additional methods, namely optical rotation method.

And that method is less sensitive and selective than the method that basically the other regulatory authorities are using.

Alicia Mundy: I'm sorry, so you said that method is less intensive?

Janet Woodcock: Less sensitive he said and selective. This is Janet Woodcock. However I would stress that there's going to be multiple levels of testing and the manufacturer - the USP and the European pharmacopeias are going to be incorporating the NMR method into their set of tests that would be required for heparin.

Karen Riley: So that NMR method is one of the two tests that we posted on our website to screen for contaminant and heparin API.

Moheb Nasr: That's correct.

Karen Riley: Anything further Alicia?

Alicia Mundy: No, thank you very much.

Karen Riley: Okay, thank you, next question please.

Coordinator: Next question is from Anna Edney, your line is open.

Karen Riley: Please identify yourself?

Anna Edney: Hi, I'm with Congress Daily. I just wanted to make sure that I was clear on the testing, if USP is going to be incorporating it, is it - it's going to go on indefinitely then, this isn't a you know month or year long testing.

Janet Woodcock: Yes. What we talked about at the regulator's meeting, the analysts and I know this may be in too much detail for some of the non-scientists, but that we need - not only do we need tests that would be ongoing for the oversulfated chondroitin sulfate, but we really want to have tests that really identify the heparin and are able to assess its purity.

That would be a very modern test, so there's a commitment around the world to institute those tests as the testing requirements for heparin.

Anna Edney: Okay, and if I can follow up, the byproduct that you mentioned that was in excess amounts in some of the heparin, in - it's just in large amounts can it be harmful at all?

Janet Woodcock: Dermatan sulfate is as usually is - can be a contaminant in heparin and it's been observed in other drug products. So we don't have results of it being harmful that we know of, however I would say it should not be present in

large amounts, it's an impurity and it should be controlled, you know kept to a small level.

So we will be instituting requirements I think for that as well.

Anna: Thank you.

Karen Riley: Thank you, next question please.

Coordinator: The next question is from Dawn Heefner, your line is open.

Dawn Heefner: Hi, thank you for taking the call, I'm Dawn Heefner, I'm with ABC in Philadelphia. My question concerns the Baxter plant. You had early on in the investigation asked or mentioned that you had inspected the plant.

Have you gone back to the Baxter plant, have you inspected any of the other plants that have also recalled their heparin? Thank you.

Janet Woodcock: I will have Deb Autor answer that question.

Deborah Autor: Yeah, we've conducted a series of inspections both in this country and in China to investigate this issue.

Dawn Heefner: Have you gone back since the initial - my follow up is have you gone back since the initial inspection, since the Chinese are now saying well gee maybe it happened here.

Deborah Autor: I will have to check unless (Joe), are you there, do you have that fact at your fingertips? He may not be on the call as a speaker. I don't think we have based

on what we understand so far I don't believe that that would send us back to Baxter at this time.

I'll look through my notes and see if I have that information and if I do I'll join back…

Janet Woodcock: Yeah, this is Janet Woodcock too, I would like to say to people, I know that people are focusing on inspection, but you know we got samples of this heparin and gave it to multiple analysts.

And even in their own laboratories, with all their analytical equipment it took them a while to find out there was anything different or wrong with these heparin samples.

So there are limitations to what inspections can tell you.

Deborah Autor: Right, and we found with respect to the Baxter product we found contamination in the active pharmaceutical ingredient that was used to supply Baxter.

So that would give us reason to think the contamination occurred before it got to Baxter.

Dawn Heefner: Okay, thank you. That answers a lot, thank you.

Karen Riley: Okay thank you, next question please.

Coordinator: Next question is from Kevin Freking, you line is open.

Kevin Freking: Hi, Kevin Freking, Associated Press. Chinese officials said this morning that there were allergic reactions in patients taking heparin that didn't have this contaminant in it, and can you say to what extent that is true?

Janet Woodcock: We had a discussion with the Chinese officials about this lot. We have tested this lot that they're referring to and have found contamination. They have a different sample and in their testing they did not find contamination.

But we are fairly certain because of multiple laboratories here doing the testing that this lot contains contaminants.

Kevin Freking: Thank you.

Karen Riley: Thank you, next question please.

Coordinator: The next question is from Miriam Falco, your line is open.

Miriam: Hi, thanks for taking the questions. I'm still a little confused about what the Chinese are claiming today and looking at the map with the eleven countries, and by the way you didn't list Japan, you do list the US in your list of countries under the map so I think that's where the discrepancy came from.

Who supplied the heparin, what manufacturer or distributor supplied the heparin to all these other countries? Because if it's not Baxter then that sort of would explain to me at least that it couldn't just have been in New Jersey.

And what's the next step in you investigation now and what's the advice you're giving patients who are hearing this and might be quite confused by this news?

Janet Woodcock: Okay, well let's start from the patient, okay. For the patients, our message is number one that heparin supply in the US is tested and is free of this contaminant.

Number two, we now feel we have a mechanistic link, so we feel that the testing requirements that we've put in place will prevent the occurrence of this event as far as the spike of events.

Okay, number three you're asking where did all this contaminated heparin around the world come from Baxter, no. It came - it - there was a variety of different firms that produced the heparin product in these different countries.

But what we're saying is that they were traced back to these different suppliers in China, okay. So at one point what we found out about heparin, talking to the worldwide regulators, is it's shipped all over the place.

And you know maybe it's made into a final dosage form in one country and then shipped to another country and so forth.

But when we ship - we look back at where the lots came from, they came from China, okay. Now I think - I believe what the Chinese authorities are saying though is something different, which is they are acknowledging there is a contaminant that originated in China, that's what we understand from them.

However they think that isn't linked to the adverse events that were observed in the US and Germany.

Karen Riley: Miriam is that good?

Miriam Falco: Yeah, that helps, thank you.

Karen Riley: And by the way that was Miriam Falco, CNN News.

Miriam Falco: Oh I'm sorry.

Karen Riley: Yes that was - next question please.

Coordinator: The next question is from Marc Kaufman your line is open.

Mark Kaufman: Thank you very much. Two questions, one has to do with - you were saying that now you believe that the contamination went back as far as 2006, if you could just walk us through a little bit how you came to that conclusion.

And the second question is this, the Chinese today made it clear that they did not believe that the problem was caused in China. From your perspective, you know on a one to ten scale or whatever, how confident are you that this is something that did occur in China?

And I guess a third question if I could slip it in is if this was done intentionally in the United States would that be a criminal act?

Janet Woodcock: I'll leave that last question for Deb Autor but to answer - we - first of all, let's all be clear, heparin should not be contaminated, all right?

Regardless of whether or not that contamination caused acute adverse events, it should not be contaminated. So that we have all agreed emanated from these plants that we've already talked about, okay?

Now we are fairly confident based on the biological information that we just very recently have, that this contaminant is capable of triggering these types of reactions, okay.

And it appears to be dose related, so it's quite likely some people would (seek) those that wouldn't get it and quite likely depending on the root of administration and the feed and the dose and everything, you know not everyone would get this reaction.

Deb, maybe you want to talk about the…

Marc Kaufman: But also the question of how confident are you that this - that the contamination occurred in China as opposed to somewhere else further down the line?

Janet Woodcock: There's no real dispute amongst anywhere about where the contamination originated, I don't think.

Marc Kaufman: Well the Chinese dispute it.

Janet Woodcock: No, they dispute that the contaminant caused the adverse events.

Marc Kaufman: Of the - okay, this morning they disputed that it had occurred in China too, but okay, never mind.

Janet Woodcock: I don't know, we had a discussion with China, the Chinese regulators at the meeting on Thursday and Friday and they have done testing and they have instituted testing in their country to prevent lots from being exported that are contaminated.

Deborah Autor: And they also said that they found their own heparin to be contaminated.

Janet Woodcock: They did.

Deborah Autor: So - and if you look at this point in time we don't know exactly where in the supply chain the contamination occurred, but if you look at the supply chain of all the contaminated products found around the world, the one thing they have in common is China.

Marc Kaufman: Okay. And how about that question I just - if this occurred in the United States and it was intentional, if they'd be adding the chondroitin, would that be a criminal act?

Deborah Autor: That would be a criminal act but again we don't have any reason to think that's what happened.

Marc Kaufman: Okay. Thank you.

Karen Riley: Okay, thank you next question please.

Coordinator: The next question is from Jon Rockoff, your line is open.

Jon Rockoff: Hi, Jon Rockoff, Baltimore Sun. Can you just talk a little bit more - I'm just thickheaded about the mechanism by which the contaminant causes these blood reactions that are the side effects that we're talking about.

Janet Woodcock: Right. This is Janet Woodcock. Well you know there are many ways that you can develop reactions as you know after you're administrated something or say you get a bee sting or you're allergic to something, right.

And you can get hypotension and we don't think it's that type of reaction, we think that - which is allergic we think this is something when where oversulfated chondroitin sulfate is injected into the blood, it causes things called mediators to be triggered.

And they can cause a wide range of things such as low blood pressure and we have observed that, and that's the scientific data we're talking about. We will publish this and I imagine other scientists will publish the other emerging data I referred to, and that will be clearer.

Obviously this data needs to be peer reviewed and it needs to be then viewed by the scientific community.

Jon Rockoff: I mean is this sort of mechanism present in other sorts of reactions like similar…

Janet Woodcock: Yes, yes.

Jon Rockoff: Like what would be sort of like an analogy.

Janet Woodcock: Well I suppose, you know they are different mechanisms, I can't get into it on the phone, but for example you know that sometimes you get contrast mediums to have your - to look at your kidney function.

And some people they get that and then they collapse, as an internist I've been called to resuscitate people like that numerous times. And you know the contrast medium that's injected into them suddenly causes them to develop low blood pressure.

Joh Rockoff: Thanks.

Janet Woodcock: Does that make sense?

Jon Rockoff: Yeah, thanks.

Karen Riley: Okay, we have time for one more call.

Coordinator: The next question is from Jyllian Kemsley, your line is open.

Jyllian Kemsley: Hi, I'm with Chemical and Engineering news. The mediators in the blood that seem to - that you believe are involved in this reaction, what is their normal role physiologically?

Janet Woodcock: I'm not sure we know. We - that's probably a little bit beyond my - beyond I think what we can talk about on this call.

But most of these - all these mediators are involved of course in the body's defense against one thing or another.

Jyllian Kemsley: So it's part of an immune response if not necessarily part of an allergic response?

Janet Woodcock: Well immune and allergic are very similar. This is not the classic immune or allergic response, in fact. But we believe many of these other responses of the body has, also, or, to, you know, maintain homeostasis in one way or another.

Karen Riley: Okay, well thank you all for participating in today's media call on FDA's ongoing heparin investigation.

We had two other technical experts who spoke today, it was Deborah Autor, D E B O R A H A U T O R. She's Director of the Office of Compliance in CDER and Moheb Nasr, M O H E B N A S R, Director of the Office of New Drug Quality Assessment in CDER

And also I want to assure everyone that the map has now been corrected. My ability to count beyond ten has been fixed.

And please I want to remind everyone that at the end of this call a replay will be available starting at - in a couple of hours, I guess 5:30 for a couple of weeks.

And if you have any additional questions please call me, Karen Riley at 301-827-6244 or even better, email me at karen.riley - R I L E Y @fda.hhs.gov.

Thank you and have a good day.

END

EXHIBIT E


NDC 0641-2450-45
Heparin
Sodium Injection, USP
1000 USP units/1 mL
℞ only
25 x 30 mL Multiple Dose Vials
FOR INTRAVENOUS OR
DEEP SUBCUTANEOUS USE
Baxter
Manufactured by Baxter Healthcare Corporation
Deerfield, IL 60015 USA
462-273-00
EXP.
LOT
04 7020
10/2008
Each mL contains heparin sodium 1000 USP units, sodium chloride 8.6 mg and benzyl alcohol 0.01 mL in Water for Injection. pH 5.0-7.5; sodium hydroxide and/or hydrochloric acid added, if needed, for pH adjustment.
DERIVED FROM PORCINE INTESTINES
Usual Dosage: See package insert for complete prescribing information.
Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature].
N 3 0641-2450-45 8